

Description

BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL VIRAL REGULATORY GENES AND USES THEREOF

BACKGROUND OF INVENTION

CONTINUATION STATEMENT

[0001] This application is a continuation of U.S. Provisional Patent Application Serial No. 60457788, filed 27-Mar-03, entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof", and is a continuation of U.S. Patent Application Serial No. 10604984, filed 29-Aug-03, entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof", and is continuation in part of U.S. Patent Application Serial No. 10604945, filed 27-Aug-03, entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof", and is a continuation in part of U.S. Patent Application Serial No. 10303778, filed 26-Nov-02,

entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof", and is a continuation in part of U.S. Provisional Patent Application Serial No. 60411230, filed 17-Jan-03, entitled "Bioinformatically Detectable Group of Novel HIV Regulatory Genes and Uses of Thereof ", and is a continuation in part of U.S. Patent Application Serial No. 10604944, filed 28-Aug-03, entitled "Bioinformatically Detectable Group of Novel HIV Regulatory Genes and Uses of Thereof ", and is a continuation in part of U.S. Provisional Patent Application Serial No. 60441241, filed 17-Jan-03, entitled "Bioinformatically Detectable Group of Novel Vaccinia Regulatory Genes and Uses of Thereof ", and is a continuation in part of U.S. Patent Application Serial No. 10604943, filed 28-Aug-03, entitled "Bioinformatically Detectable Group of Novel Vaccinia Regulatory Genes and Uses of Thereof", and is a continuation in part of U.S. Patent Application Serial No. 10604942, filed 27-Aug-03, entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof", and is a continuation in part of U.S. Patent Application Serial No. 10310188, filed 5-Dec-02, entitled "Bioinformatically Detectable Group of Novel Viral Regulatory Genes and Uses of Thereof ", and is a continu-

ation in part of U.S Patent Application Serial No. 10605838, filed 30-Oct-03, entitled "Bioinformatically Detectable Group of Novel HIV Regulatory Genes and Uses of Thereof", and is a continuation in part of U.S Patent Application Serial No. 10605840, filed 30-Oct-03, entitled "Bioinformatically Detectable Group of Novel Vaccinia Regulatory Genes and Uses of Thereof", the disclosures of which applications are all hereby incorporated by reference and claims priority therefrom

FIELD OF THE INVENTION

[0002] The present invention relates to a group of bioinformatically detectable novel viral RNA regulatory genes, here identified as "viral genomic address messenger" or "VGAM" genes.

DESCRIPTION OF PRIOR ART

[0003] Small RNAs are known to perform diverse cellular functions, including post-transcriptional gene expression regulation. The first two such RNA genes, Lin-4 and Let-7, were identified by genetic analysis of *Caenorhabditis Elegans* (*Elegans*) developmental timing, and were termed short temporal RNA (stRNA) (Wightman, B., Ha, I., Ruvkun, G., *Cell* 75, 855 (1993); Erdmann, V.A. et al., *Nucleic*

Acids Res. 29, 189 (2001); Lee, R. C., Feinbaum, R. L., Ambros, V., Cell 75, 843 (1993); Reinhart, B. et al., Nature 403, 901 (2000)).

[0004] Lin-4 and Let-7 each transcribe a ~22 nucleotide (nt) RNA, which acts a post transcriptional repressor of target mRNAs, by binding to elements in the 3'-untranslated region (UTR) of these target mRNAs, which are complimentary to the 22 nt sequence of Lin-4 and Let-7 respectively. While Lin-4 and Let-7 are expressed at different developmental stage, first larval stage and fourth larval stage respectively, both specify the temporal progression of cell fates, by triggering post-transcriptional control over other genes (Wightman, B., Ha, I., Ruvkun, G., Cell 75, 855 (1993); Slack et al., Mol.Cell 5 ,659 (2000)). Let-7 as well as its temporal regulation have been demonstrated to be conserved in all major groups of bilaterally symmetrical animals, from nematodes, through flies to humans (Pasquinelli, A., et al. Nature 408 ,86 (2000)).

[0005] The initial transcription product of Lin-4 and Let-7 is a ~60-80nt RNA, the nucleotide sequence of the first half of which is partially complimentary to that of its second half, therefore allowing this RNA to fold onto itself, forming a "hairpin structure". The final gene product is a ~22nt RNA,

which is "diced" from the above mentioned "hairpin structure", by an enzyme called Dicer, which also apparently also mediates the complimentary binding of this ~22nt segment to a binding site in the 3' UTR of its target gene.

[0006] Recent studies have uncovered 93 new genes in this class, now referred to as micro RNA or miRNA genes, in genomes of *Elegans*, *Drosophila*, and Human (Lagos-Quintana, M., Rauhut, R., Lendeckel, W., Tuschl, T., *Science* 294 ,853 (2001); Lau, N.C., Lim, L.P., Weinstein, E.G., Bartel, D.P., *Science* 294 ,858 (2001); Lee, R.C., Ambros, V., *Science* 294 ,862 (2001). Like the well studied Lin-4 and Let-7, all newly found MIR genes produce a ~60–80nt RNA having a nucleotide sequence capable of forming a "hairpin structure". Expressions of the precursor ~60–80nt RNA and of the resulting diced ~22nt RNA of most of these newly discovered MIR genes have been detected.

[0007] Based on the striking homology of the newly discovered MIR genes to their well-studied predecessors Lin-4 and Let-7, the new MIR genes are believed to have a similar basic function as that of Lin-4 and Let-7: modulation of target genes by complimentary binding to the UTR of these target genes, with special emphasis on modulation

of developmental control processes. This is despite the fact that the above mentioned recent studies did not find target genes to which the newly discovered MIR genes complementarily bind. While existing evidence suggests that the number of regulatory RNA genes "may turn out to be very large, numbering in the hundreds or even thousands in each genome", detecting such genes is challenging (Ruvkun G., "Perspective: Glimpses of a tiny RNA world", Science 294 ,779 (2001)).

[0008] The ability to detect novel RNA genes is limited by the methodologies used to detect such genes. All RNA genes identified so far either present a visibly discernable whole body phenotype, as do Lin-4 and Let-7 (Wightman et. al., Cell 75, 855 (1993); Reinhart et al., Nature 403, 901 (2000)), or produce significant enough quantities of RNA so as to be detected by the standard biochemical genomic techniques, as do the 93 recently detected miRNA genes. Since a limited number clones were sequenced by the researchers discovering these genes, 300 by Bartel and 100 by Tuschl (Bartel et. al., Science 294 ,858 (2001); Tuschl et. al., Science 294 ,853 (2001)), the RNA genes found can not be much rarer than 1% of all RNA genes. The recently detected miRNA genes therefore represent the more

prevalent among the miRNA gene family.

[0009] Current methodology has therefore been unable to detect RNA genes which either do not present a visually discernable whole body phenotype, or are rare (e.g. rarer than 0.1% of all RNA genes), and therefore do not produce significant enough quantities of RNA so as to be detected by standard biochemical technique. To date, miRNA have not been detected in viruses.

SUMMARY OF INVENTION

[0010] The present invention relates to a novel group of bioinformatically detectable, viral regulatory RNA genes, which repress expression of host target host genes, by means of complementary hybridization to binding sites in untranslated regions of these host target host genes. It is believed that this novel group of viral genes represent a pervasive viral mechanism of attacking hosts, and that therefore knowledge of this novel group of viral genes may be useful in preventing and treating viral diseases.

[0011] In various preferred embodiments, the present invention seeks to provide improved method and system for detection and prevention of viral disease, which is mediated by this group of novel viral genes.

[0012] Accordingly, the invention provides several substantially

pure nucleic acids (e.g., genomic nucleic acid, cDNA or synthetic nucleic acid) each encoding a novel viral gene of the VGAM group of gene, vectors comprising the nucleic acids , probes comprising the nucleic acids , a method and system for selectively modulating translation of known "target" genes utilizing the vectors, and a method and system for detecting expression of known "target" genes utilizing the probe.

[0013] By "substantially pure nucleic acid" is meant nucleic acid that is free of the genes which, in the naturally-occurring genome of the organism from which the nucleic acid of the invention is derived, flank the genes discovered and isolated by the present invention. The term therefore includes, for example, a recombinant nucleic acid which is incorporated into a vector, into an autonomously replicating plasmid or virus, or into the genomic nucleic acid of a prokaryote or eukaryote at a site other than its natural site; or which exists as a separate molecule (e.g., a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences. It also includes a recombinant nucleic acid which is part of a hybrid gene encoding additional polypeptide sequence.

[0014] "Inhibiting translation" is defined as the ability to prevent synthesis of a specific protein encoded by a respective gene, by means of inhibiting the translation of the mRNA of this gene. "Translation inhibitor site" is defined as the minimal nucleic acid sequence sufficient to inhibit translation.

[0015] There is thus provided in accordance with a preferred embodiment of the present invention a bioinformatically detectable novel viral gene encoding substantially pure nucleic acid wherein: RNA encoded by the bioinformatically detectable novel viral gene is about 18 to about 24 nucleotides in length, and originates from an RNA precursor, which RNA precursor is about 50 to about 120 nucleotides in length, a nucleotide sequence of a first half of the RNA precursor is a partial inversed-reversed sequence of a nucleotide sequence of a second half thereof, a nucleotide sequence of the RNA encoded by the novel viral gene is a partial inversed-reversed sequence of a nucleotide sequence of a binding site associated with at least one host target gene, and a function of the novel viral gene is bioinformatically deducible.

[0016] There is further provided in accordance with another preferred embodiment of the present invention a method for

anti-viral treatment comprising neutralizing said RNA.

[0017] Further in accordance with a preferred embodiment of the present invention the neutralizing comprises: synthesizing a complementary nucleic acid molecule, a nucleic sequence of which complementary nucleic acid molecule is a partial inversed-reversed sequence of said RNA, and transfecting host cells with the complementary nucleic acid molecule, thereby complementarily binding said RNA.

[0018] Further in accordance with a preferred embodiment of the present invention the neutralizing comprises immunologically neutralizing.

[0019] There is still further provided in accordance with another preferred embodiment of the present invention a bioinformatically detectable novel viral gene encoding substantially pure nucleic acid wherein: RNA encoded by the bioinformatically detectable novel viral gene includes a plurality of RNA sections, each of the RNA sections being about 50 to about 120 nucleotides in length, and including an RNA segment, which RNA segment is about 18 to about 24 nucleotides in length, a nucleotide sequence of a first half of each of the RNA sections encoded by the novel viral gene is a partial inversed-reversed sequence of nucleotide sequence of a second half thereof, a nucleotide

sequence of each of the RNA segments encoded by the novel viral gene is a partial inversed–reversed sequence of the nucleotide sequence of a binding site associated with at least one target host gene, and a function of the novel viral gene is bioinformatically deducible from the following data elements: the nucleotide sequence of the RNA encoded by the novel viral gene, a nucleotide sequence of the at least one target host gene, and function of the at least one target host gene.

[0020] Further in accordance with a preferred embodiment of the present invention the function of the novel viral gene is bioinformatically deducible from the following data elements: the nucleotide sequence of the RNA encoded by the bioinformatically detectable novel viral gene, a nucleotide sequence of the at least one target host gene, and a function of the at least one target host gene.

[0021] Still further in accordance with a preferred embodiment of the present invention the RNA encoded by the novel viral gene complementarily binds the binding site associated with the at least one target host gene, thereby modulating expression of the at least one target host gene.

[0022] Additionally in accordance with a preferred embodiment of the present invention the binding site associated with

at least one target host gene is located in an untranslated region of RNA encoded by the at least one target host gene.

[0023] Moreover in accordance with a preferred embodiment of the present invention the function of the novel viral gene is selective inhibition of translation of the at least one target host gene, which selective inhibition includes complementary hybridization of the RNA encoded by the novel viral gene to the binding site.

[0024] Further in accordance with a preferred embodiment of the present invention the invention includes a vector including the DNA.

[0025] Still further in accordance with a preferred embodiment of the present invention the invention includes a method of selectively inhibiting translation of at least one gene, including introducing the vector.

[0026] Moreover in accordance with a preferred embodiment of the present invention the introducing includes utilizing RNAi pathway.

[0027] Additionally in accordance with a preferred embodiment of the present invention the invention includes a gene expression inhibition system including: the vector, and a vector inserter, functional to insert the vector into a cell,

thereby selectively inhibiting translation of at least one gene.

[0028] Further in accordance with a preferred embodiment of the present invention the invention includes a probe including the DNA.

[0029] Still further in accordance with a preferred embodiment of the present invention the invention includes a method of selectively detecting expression of at least one gene, including using the probe.

[0030] Additionally in accordance with a preferred embodiment of the present invention the invention includes a gene expression detection system including: the probe, and a gene expression detector functional to selectively detect expression of at least one gene.

[0031] Further in accordance with a preferred embodiment of the present invention the invention includes an anti-viral substance capable of neutralizing the RNA.

[0032] Still further in accordance with a preferred embodiment of the present invention the neutralizing includes complementarily binding the RNA.

[0033] Additionally in accordance with a preferred embodiment of the present invention the neutralizing includes immunologically neutralizing.

- [0034] Moreover in accordance with a preferred embodiment of the present invention the invention includes a method for anti-viral treatment including neutralizing the RNA.
- [0035] Further in accordance with a preferred embodiment of the present invention the neutralizing includes: synthesizing a complementary nucleic acid molecule, a nucleic sequence of which complementary nucleic acid molecule is a partial inversed-reversed sequence of the RNA, and transfecting host cells with the complementary nucleic acid molecule, thereby complementarily binding the RNA.
- [0036] Still further in accordance with a preferred embodiment of the present invention the neutralizing includes immuno-logically neutralizing.

BRIEF DESCRIPTION OF DRAWINGS

- [0037] Fig. 1 is a simplified diagram illustrating a mode by which viral genes of a novel group of viral genes of the present invention, modulate expression of known host target genes;
- [0038] Fig. 2 is a simplified block diagram illustrating a bioinformatic gene detection system capable of detecting genes of the novel group of genes of the present invention, which system is constructed and operative in accordance with a preferred embodiment of the present invention;

- [0039] Fig. 3 is a simplified flowchart illustrating operation of a mechanism for training of a computer system to recognize the novel genes of the present invention, which mechanism is constructed and operative in accordance with a preferred embodiment of the present invention;
- [0040] Fig. 4A is a simplified block diagram of a non-coding genomic sequence detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0041] Fig. 4B is a simplified flowchart illustrating operation of a non-coding genomic sequence detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0042] Fig. 5A is a simplified block diagram of a hairpin detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0043] Fig. 5B is a simplified flowchart illustrating operation of a hairpin detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0044] Fig. 6A is a simplified block diagram of a dicer-cut location detector constructed and operative in accordance with a preferred embodiment of the present invention;
- [0045] Fig. 6B is a simplified flowchart illustrating training of a

dicer-cut location detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0046] Fig. 7A is a simplified block diagram of a target-gene binding-site detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0047] Fig. 7B is a simplified flowchart illustrating operation of a target-gene binding-site detector constructed and operative in accordance with a preferred embodiment of the present invention;

[0048] Fig. 8 is a simplified flowchart illustrating operation of a function & utility analyzer constructed and operative in accordance with a preferred embodiment of the present invention;

[0049] Fig. 9 is a simplified diagram describing a novel bioinformatically detected group of regulatory viral genes, referred to here as Viral Genomic Record (VGR) genes, each of which encodes an "operon-like" cluster of novel viral miRNA-like genes, which in turn modulates expression of a plurality of host target genes;

[0050] Fig. 10 is a block diagram illustrating different utilities of genes of a novel group of genes, and operons of a novel

group of operons, both of the present invention;

[0051] Figs. 11A and 11B are simplified diagrams, which when taken together illustrate a mode of gene therapy applicable to genes of the novel group of genes of the present invention;

[0052] Fig. 12A is an annotated sequence of EST72223 comprising novel gene GAM24 detected by the gene detection system of the present invention;

[0053] Figs. 12B and 12C are pictures of laboratory results, which when taken together demonstrate laboratory confirmation of expression of the bioinformatically detected novel gene GAM24 of Fig. 12A;

[0054] Fig. 12D provides pictures of laboratory results, which when taken together demonstrate further laboratory confirmation of expression of the bioinformatically detected novel gene GAM24 of Fig. 12A;

[0055] Fig. 13A is an annotated sequence of an EST7929020 comprising novel genes GAM23 and GAM25 detected by the gene detection system of the present invention;

[0056] Fig. 13B is a picture of laboratory results, which confirm expression of bioinformatically detected novel genes GAM23 and GAM25 of Fig. 13A;

[0057] Fig. 13C is a picture of laboratory results, which confirm

endogenous expression of bioinformatically detected novel gene GAM25 of Fig. 15A;

[0058] Fig. 14A is an annotated sequence of an EST1388749 comprising novel gene GAM26 detected by the gene detection system of the present invention;

[0059] Figs. 14B is a picture of laboratory results, which confirm expression of the bioinformatically detected novel gene GAM26 of Fig. 14A;

BRIEF DESCRIPTION OF SEQUENCES

[0060] A Sequence Listing of genomic sequences of the present invention designated SEQ ID:1 through SEQ ID:46755 is attached to this application. The genomic listing comprises the following nucleotide sequences: Genomic sequences designated SEQ ID:1 through SEQ ID:2725 are nucleotide sequences of 2725 gene precursors of respective novel genes of the present invention; Genomic sequences designated SEQ ID:2726 through SEQ ID:5450 are nucleotide sequences of 2725 genes of the present invention; and Genomic sequences designated SEQ ID:5451 through SEQ ID:46755 are nucleotide sequences of 41305 host target binding sites.

DETAILED DESCRIPTION

[0061] Reference is now made to Fig. 1 which is a simplified diagram illustrating a mode by which genes of a novel group of viral genes of the present invention, modulate expression of known host target genes.

[0062] The novel genes of the present invention are viral micro RNA (miRNA)-like, regulatory RNA genes, modulating expression of known host target genes. This mode of modulation is common to other known miRNA genes, as described hereinabove with reference to the background of the invention section.

[0063] VGAM GENE is a viral gene contained in the virus genome and TARGET GENE is a human gene contained in the DNA of the human genome.

[0064] VGAM GENE encodes a VGAM PRECURSOR RNA. However, similar to other miRNA genes, and unlike most ordinary genes, its RNA, VGAM PRECURSOR RNA, does not encode a protein.

[0065] VGAM PRECURSOR RNA folds onto itself, forming VGAM FOLDED PRECURSOR RNA. As Fig.1 illustrates, VGAM FOLDED PRECURSOR RNA forms a "hairpin structure" folding onto itself. As is well known in the art, this "hairpin structure" is typical genes of the miRNA genes, and is due to the fact that nucleotide sequence of the first half of the

RNA of a gene in this group is an accurate or partial inverted-reversed sequence of the nucleotide sequence of its second half. By "inverted-reversed" is meant a sequence which is reversed and wherein each nucleotide is replaced by a complementary nucleotide, as is well known in the art (e.g. ATGGC is the inverted-reversed sequence of GCCAT).

[0066] An enzyme complex, designated DICER COMPLEX, "dices" the VGAM FOLDED PRECURSOR RNA into a single stranded RNA segment, about 22 nucleotides long, designated VGAM RNA. As is known in the art, "dicing" of the hairpin structured RNA precursor into shorter RNA segments about 22 nucleotides long by a Dicer type enzyme is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins.

[0067] VGAM HOST TARGET GENE encodes a corresponding messenger RNA, designated VGAM HOST TARGET RNA. This VGAM HOST TARGET RNA comprises three regions: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[0068] VGAM RNA binds complementarily a BINDING SITE, located on the 3'UTR segment of TARGET RNA. This complemen-

tarily binding is due to the fact that the nucleotide sequence of VGAM RNA is an accurate or partial inversed-reversed sequence of the nucleotide sequence of BINDING SITE.

[0069] The complimentary binding of VGAM RNA to BINDING SITE inhibits translation of VGAM HOST TARGET RNA into VGAM HOST TARGET PROTEIN. VGAM HOST TARGET PROTEIN is therefore outlined by a broken line.

[0070] It is appreciated by one skilled in the art that the mode of transcriptional inhibition illustrated by Fig. 1 with specific reference to VGAM genes of the present invention, is in fact common to all other miRNA genes. A specific complimentary binding site has been demonstrated only for Lin-4 and Let-7. All the other 93 newly discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complimentary binding, although specific complimentary binding sites for these genes have not yet been found (Ruvkun G., "Perspective: Glimpses of a tiny RNA world", Science 294 ,779 (2001)). The present invention discloses a novel group of viral genes, the VGAM genes, belonging to the miRNA genes group, and for which a specific an complimentary binding has been determined.

[0071] Reference is now made to Fig. 2 which is a simplified block diagram illustrating a bioinformatic gene detection system capable of detecting genes of the novel group of genes of the present invention, which system is constructed and operative in accordance with a preferred embodiment of the present invention.

[0072] A centerpiece of the present invention is a bioinformatic gene detection engine 100, which is a preferred implementation of a mechanism capable of bioinformatically detecting genes of the novel group of genes of the present invention.

[0073] The function of the bioinformatic gene detection engine 100 is as follows: it receives three types of input, expressed RNA data 102, sequenced DNA data 104, and protein function data 106, performs a complex process of analysis of this data as elaborated below, and based on this analysis produces output of a bioinformatically detected group of novel genes designated 108.

[0074] Expressed RNA data 102 comprises published expressed sequence tags (EST) data, , published mRNA data, as well as other sources of published RNA data. Sequenced DNA data 104 comprises alphanumeric data describing sequenced genomic data, which preferably includes annota-

tion data such as location of known protein coding regions relative to the sequenced data. Protein function data 106 comprises scientific publications reporting studies which elucidated physiological function known proteins, and their connection, involvement and possible utility in treatment and diagnosis of various diseases. Expressed RNA data 102, sequenced DNA data 104 may preferably be obtained from data published by the National Center for Bioinformatics (NCBI) at the National Institute of Health (NIH), as well as from various other published data sources. Protein function data 106 may preferably be obtained from any one of numerous relevant published data sources, such as the Online Mendelian Inherited Disease In Man (OMIM) database developed by John Hopkins University, and also published by NCBI.

[0075] Prior to actual detection of bioinformatically detected novel genes 108 by the bioinformatic gene detection engine 100, a process of bioinformatic gene detection engine training & validation designated 110 takes place. This process uses the known miRNA genes as a training set (some 200 such genes have been found to date using biological laboratory means), to train the bioinformatic gene detection engine 100 to bioinformatically recognize

miRNA-like genes, and their respective potential target binding sites. Bioinformatic gene detection engine training & validation 110 is further describe hereinbelow with reference to Fig. 3.

[0076] The bioinformatic gene detection engine 100 comprises several modules which are preferably activated sequentially, and are described as follows:

[0077] A non-coding genomic sequence detector 112 operative to bioinformatically detect non-protein coding genomic sequences. The non-coding genomic sequence detector 112 is further described hereinbelow with reference to Figs. 4A and 4B.

[0078] A hairpin detector 114 operative to bioinformatically detect genomic "hairpin-shaped" sequences, similar to VGAM FOLDED PRECURSOR of Fig. 1. The hairpin detector 114 is further described hereinbelow with reference to Figs. 5A and 5B.

[0079] A dicer-cut location detector 116 operative to bioinformatically detect the location on a hairpin shaped sequence which is enzymatically cut by DICER COMPLEX of Fig. 1. The dicer-cut location detector 116 is further described hereinbelow with reference to Fig. 6A.

[0080] A target-gene binding-site detector 118 operative to

bioinformatically detect host target having binding sites, the nucleotide sequence of which is partially complementary to that of a given genomic sequence, such as a sequence cut by DICER COMPLEX of Fig. 1. The target-gene binding-site detector 118 is further described hereinbelow with reference to Figs. 7A and 7B.

[0081] A function & utility analyzer 120 operative to analyze function and utility of host target, in order to identify host target which have a significant clinical function and utility. The function & utility analyzer 120 is further described hereinbelow with reference to Fig. 8.

[0082] Hardware implementation of the bioinformatic gene detection engine 100 is important, since significant computing power is preferably required in order to perform the computation of bioinformatic gene detection engine 100 in reasonable time and cost. As an example, it is estimated that using one powerful 8-processor PC Server, over 30 months of computing time (at 24 hours per day) would be required in order to detect all miRNA genes in human EST data, and their respective binding sites.

[0083] For example, in order to address this challenge at reasonable time and cost, a preferred embodiment of the present invention may comprise a cluster of a large num-

ber of personal computers (PCs), such as 100 PCs (Pentium IV, 1.7GHz, with 40GB storage each), connected by Ethernet to several strong servers, such as 4 servers (2-CPU, Xeon 2.2GHz, with 200GB storage each), combined with an 8-processor server (8-CPU, Xeon 550Mhz w/ 8GB RAM) connected via 2 HBA fiber-channels to an EMC Clariion 100-disks, 3.6 Terabyte storage device. Additionally, preferably an efficient database computer program, such as Microsoft (TM) SQL-Server database computer program is used and is optimized to the specific requirements of bioinformatic gene detection engine 100. Furthermore, the PCs are preferably optimized to operate close to 100% CPU usage continuously, as is known in the art. Using suitable hardware and software may preferably reduce the required calculation time in the abovementioned example from 30 months to 20 days.

[0084] It is appreciated that the abovementioned hardware configuration is not meant to be limiting, and is given as an illustration only. The present invention may be implemented in a wide variety of hardware and software configurations.

[0085] The present invention discloses 2725 novel viral genes of the VGAM group of genes, which have been detected

bioinformatically, as described hereinbelow with reference to Fig. 1 through Fig. 8. Laboratory confirmation of 4 genes of the GAM group of genes is described hereinbelow with reference to Figs. 12 through 14.

[0086] Reference is now made to Fig. 3 which is a simplified flowchart illustrating operation of a mechanism for training of a computer system to recognize the novel genes of the present invention. This mechanism is a preferred implementation of the bioinformatic gene detection engine training & validation 110 described hereinabove with reference to Fig. 2.

[0087] Bioinformatic gene detection engine training & validation 110 of Fig. 2 begins by training the bioinformatic gene detection engine to recognize known miRNA genes, as designated by numeral 122. This training step comprises hairpin detector training & validation 124, further described hereinbelow with reference to Fig. 12 A, dicer-cut location detector training & validation 126, further described hereinbelow with reference to Fig. 6A and 6B, and target-gene binding-site detector training & validation 128, further described hereinbelow with reference to Fig. 7A.

[0088] Next, the bioinformatic gene detection engine 100 is used

to bioinformatically detect sample novel genes, as designated by numeral 130. An example of a sample novel gene thus detected is described hereinbelow with reference to Fig. 12.

[0089] Finally, wet lab experiments are preferably conducted in order to validate expression and preferably function the sample novel genes detected by the bioinformatic gene detection engine 100 in the previous step. An example of wet-lab validation of the abovementioned sample novel gene bioinformatically detected by the system is described hereinbelow with reference to Figs. 13A and 13B.

[0090] Reference is now made to Fig. 4A which is a simplified block diagram of a preferred implementation of the non-coding genomic sequence detector 112 described hereinabove with reference to Fig. 2. Non-protein coding genomic sequence detector 112 of Fig. 2 preferably receives as input at least two types of published genomic data: expressed RNA data 102, including EST data and mRNA data, and sequenced DNA data 104. After its initial training, indicated by numeral 134, and based on the abovementioned input data, the non-protein coding genomic sequence detector 112 produces as output a plurality of non-protein coding genomic sequences 136. Preferred

operation of the non-protein coding genomic sequence detector 112 is described hereinbelow with reference to Fig. 4B.

[0091] Reference is now made to Fig. 4B which is a simplified flowchart illustrating a preferred operation of the non-coding genomic sequence detector 112 of Fig. 2. Detection of non-protein coding genomic sequences to be further analyzed by the system generally preferably progresses in one of the following two paths.

[0092] A first path for detecting non-protein coding genomic sequences begins by receiving a plurality of known RNA sequences, such as EST data. Each RNA sequence is first compared to all known protein-coding sequences, in order to select only those RNA sequences which are non-protein coding. This can preferably be performed by BLAST comparison of the RNA sequence to known protein coding sequences. The abovementioned BLAST comparison to the DNA preferably also provides the localization of the RNA on the DNA.

[0093] Optionally, an attempt may be made to "expend" the non-protein RNA sequences thus found, by searching for transcription start and end signals, upstream and downstream of location of the RNA on the DNA respectively, as is well

known in the art.

[0094] A second path for detecting non-protein coding genomic sequences starts by receiving DNA sequences. The DNA sequences are parsed into non protein coding sequences, based on published DNA annotation data: extracting those DNA sequences which are between known protein coding sequences. Next, transcription start and end signals are sought. If such signals are found, and depending on their "strength", probable expressed non-protein coding genomic sequences are yielded.

[0095] Reference is now made to Fig. 5A which is a simplified block diagram of a preferred implementation of the hairpin detector 114 described hereinabove with reference to Fig. 2.

[0096] The goal of the hairpin detector 114 is to detect "hairpin" shaped genomic sequences, similar to those of known miRNA genes. As mentioned hereinabove with reference to Fig. 1, a "hairpin" genomic sequence refers to a genomic sequence which "folds onto itself" forming a hairpin like shape, due to the fact that nucleotide sequence of the first half of the nucleotide sequence is an accurate or

[0097] The hairpin detector 114 of Fig. 2 receives as input a plurality of non-protein coding genomic sequences 136 of

Fig. 4A, and after a phase of hairpin detector training & validation 124 of Fig. 3, is operative to detect and output "hairpin shaped" sequences found in the input expressed non-protein coding sequences, designated by numeral 138.

[0098] The phase of hairpin detector training & validation 124 is an iterative process of applying the hairpin detector 114 to known hairpin shaped miRNA genes, calibrating the hairpin detector 114 such that it identifies the training set of known hairpins, as well as sequences which are similar thereto. Preferred operation of the hairpin detector 114 is described hereinbelow with reference to Fig. 5B.

[0099] Reference is now made to Fig. 5B which is a simplified flowchart illustrating a preferred operation of the hairpin detector 114 of Fig. 2.

[0100] A hairpin structure is a two dimensional folding structure, resulting from the nucleotide sequence pattern: the nucleotide sequence of the first half of the hairpin sequence is an inversed-reversed sequence of the second half thereof. Different methodologies are known in the art for detection of various two dimensional and three dimensional hairpin structures.

[0101] In a preferred embodiment of the present invention, the

hairpin detector 114 initially calculates possible 2-dimensional (2D) folding patterns of a given one of the non-protein coding genomic sequences 136, preferably using a 2D folding algorithm based on free-energy calculation, such as the Zucker algorithm, as is well known in the art.

[0102] Next, the hairpin detector 114 analyzes the results of the 2D folding, in order to determine the presence, and location of hairpin structures. A 2D folding algorithm typically provides as output a listing of the base-pairing of the 2D folded shape, i.e. a listing of which all two pairs of nucleotides in the sequence which will bond. The goal of this second step, is to assess this base-pairing listing, in order to determine if it describes a hairpin type bonding pattern.

[0103] The hairpin detector 114 then assess those hairpin structures found by the previous step, comparing them to hairpins of known miRNA genes, using various parameters such as length, free-energy, amount and type of mismatches, etc. Only hairpins that bear statistically significant resemblance of the population of hairpins of known miRNAs, according to the abovementioned parameters are accepted.

[0104] Lastly, the hairpin detector 114 attempts to select those hairpin structures which are as stable as the hairpins of known miRNA genes. This may be achieved in various manners. A preferred embodiment of the present invention utilizes the following methodology comprising three steps:

[0105] First, the hairpin detector 114 attempts to group potential hairpins into "families" of closely related hairpins. As is known in the art, a free-energy calculation algorithm, typically provides multiple "versions" each describing a different possible 2D folding pattern for the given genomic sequence, and the free energy of such possible folding. The hairpin detector 114 therefore preferably assesses all hairpins found on all "versions", grouping hairpins which appear in different versions, but which share near identical locations into a common "family" of hairpins. For example, all hairpins in different versions, the center of which is within 7 nucleotides of each other may preferably be grouped to a single "family".

[0106] Next, hairpin "families" are assessed, in order to select only those families which represent hairpins that are as stable as those of known miRNA hairpins. For example, preferably only families which are represented in at least

65% of the free-energy calculation 2D folding versions, are considered stable.

[0107] Finally, an attempt is made to select the most suitable hairpin from each selected family. For example, preferably the hairpin which appears in more versions than other hairpins, and in versions the free-energy of which is lower, may be selected.

[0108] Reference is now made to Fig. 6A which is a simplified block diagram of a preferred implementation of the dicer-cut location detector 116 described hereinabove with reference to Fig. 2.

[0109] The goal of the dicer-cut location detector 116 is to detect the location in which DICER COMPLEX of Fig. 1, comprising the enzyme Dicer, would "dice" the given hairpin sequence, similar to VGAM FOLDED PRECURSOR RNA, yielding VGAM RNA both of Fig. 1.

[0110] The dicer-cut location detector 116 of Fig. 2 therefore receives as input a plurality of hairpins on genomic sequences 138 of Fig. 5A, which were calculated by the previous step, and after a phase of dicer-cut location detector training & validation 126 of Fig. 3, is operative to detect a respective plurality of dicer-cut sequences from hairpins 140, one for each hairpin.

[0111] In a preferred embodiment of the present invention, the dicer-cut location detector 116 preferably uses a combination of neural networks, Bayesian networks, Markovian modeling, and Support Vector Machines (SVMs) trained on the known dicer-cut locations of known miRNA genes, in order to detect dicer-cut locations. Dicer-cut location detector training & validation 126, which is further described hereinbelow with reference to Fig. 6B.

[0112] Reference is now made to Fig. 6 B which is a simplified flowchart illustrating a preferred implementation of dicer-cut location detector training & validation 126 of Fig. 3. Dicer-cut location detector 116 first preprocesses known miRNA hairpins and their respective dicer-cut locations, so as to be able to properly analyze them and train the detection system accordingly:

[0113] The folding pattern is calculated for each known miRNA, preferably based on free-energy calculation, and the size of the hairpin, the size of the loop at the center of the hairpin, and "bulges" (i.e. mismatched base-pairs) in the folded hairpin are noted.

[0114] The dicer-cut location, which is known for known miRNA genes, is noted relative to the above, as well as to the nucleotides in each location along the hairpin. Frequency of

identity of nucleotides, and nucleotide-pairing, relative to their location in the hairpin, and relative to the known dicer-cut location in the known miRNA genes is analyzed and modeled.

[0115] Different techniques are well known in the art for analysis of existing pattern from a given "training set" of species belonging to a genus, which techniques are then capable, to a certain degree, to detect similar patterns in other species not belonging to the training-set genus. Such techniques include, but are not limited to neural networks, Bayesian networks, Support Vector Machines (SVM), Genetic Algorithms, Markovian modeling, and others, as is well known in the art.

[0116] Using such techniques, preferably a combination of several of the above techniques, the known hairpins are represented as a several different networks (such as neural, Bayesian, or SVM) input and output layers. Both nucleotide, and "bulge" (i.e. nucleotide pairing or mismatch) are represented for each position in the hairpin, at the input layer, and a corresponding true/false flag at each position, indicating whether it was diced by dicer at the output layer. Multiple networks are preferably used concurrently, and the results therefrom are integrated and fur-

ther optimized. Markovian modeling may also be used to validate the results and enhance their accuracy. Finally, the bioinformatic detection of dicer-cut location of a sample novel is confirmed by wet-lab experimentation.

[0117] Reference is now made to Fig. 7A which is a simplified block diagram of a preferred implementation of the target-gene binding-site detector 118 described herein-above with reference to Fig. 2. The goal of the target-gene binding-site detector 118 is to detect a BINDING SITE of Fig. 1, located in an untranslated region of the RNA of a known gene, the nucleotide sequence of which BINDING SITE is at least partially complementary to that of a VGAM RNA of Fig. 1, thereby determining that the abovementioned known gene is a target gene of VGAM of Fig. 1.

[0118] The target-gene binding-site detector 118 of Fig. 2 therefore receives as input a plurality of dicer-cut sequences from hairpins 140 of Fig. 6A which were calculated by the previous step, and a plurality of potential target gene sequences 142 which derive sequence DNA data 104 of Fig. 2, and after a phase of target-gene binding-site detector training & validation 128 of Fig. 3, is operative to detect target-genes having binding site/s 144 the

nucleotide sequence of which is at least partially complementary to that of each of the plurality of dicer-cut sequences from hairpins 140. Preferred operation of the target-gene binding-site detector is further described hereinbelow with reference to Fig. 7B.

[0119] Reference is now made to Fig. 7B which is a simplified flowchart illustrating a preferred operation of the target-gene binding-site detector 118 of Fig. 2. In a preferred embodiment of the present invention, the target-gene binding-site detector 118 first performs a BLAST comparison of the nucleotide sequence of each of the plurality of dicer-cut sequences from hairpins 140, to the potential target gene sequences 142, in order to find crude potential matches. Blast results are then filtered to results which are similar to those of known binding sites (e.g. binding sites of miRNA genes Lin-4 and Let-7 to target genes Lin-14, Lin-41, Lin 28 etc.). Next the binding site is expanded, checking if nucleotide sequenced immediately adjacent to the binding site found by BLAST, may improve the match. Suitable binding sites, then are computed for free-energy and spatial structure. The results are analyzed, selecting only those binding sites, which have free-energy and spatial structure similar to that of known

binding sites.

[0120] Reference is now made to Fig. 8 which is a simplified flowchart illustrating a preferred operation of the function & utility analyzer 120 described hereinabove with reference to Fig. 2. The goal of the function & utility analyzer 120 is to determine if a potential target gene is in fact a valid clinically useful target gene. Since a potential novel VGAM gene binding a binding site in the UTR of a target gene is understood to inhibit expression of that target gene, and if that target gene is shown to have a valid clinical utility, then in such a case it follows that the potential novel gene itself also has a valid useful function which is the opposite of that of the target gene.

[0121] The function & utility analyzer 120 preferably receives as input a plurality of potential novel target genes having binding-site/s 144, generated by the target-gene binding-site detector 118, both of Fig. 7A. Each potential gene, is evaluated as follows:

[0122] First the system first checks to see if the function of the potential target gene is scientifically well established. Preferably, this can be achieved bioinformatically by searching various published data sources presenting information on known function of proteins. Many such data

sources exist and are published as is well known in the art.

[0123] Next, for those target genes the function of which is scientifically known and is well documented, the system then checks if scientific research data exists which links them to known diseases. For example, a preferred embodiment of the present invention utilizes the OMIM(TM) database published by NCBI, which summarizes research publications relating to genes which have been shown to be associated with diseases.

[0124] Finally, the specific possible utility of the target gene is evaluated. While this process too may be facilitated by bioinformatic means, it might require human evaluation of published scientific research regarding the target gene, in order to determine the utility of the target gene to the diagnosis and or treatment of specific disease. Only potential novel genes, the target-genes of which have passed all three examinations, are accepted as novel genes.

[0125] Reference is now made to Fig. 9, which is a simplified diagram describing a novel bioinformatically detected group of regulatory genes, referred to here as Viral Genomic Record (VGR) genes, that encode an "operon-like" cluster of novel viral miRNA-like genes, each modulating expres-

sion of a plurality of host target genes, the function and utility of which target genes is known.

[0126] VGR GENE (Viral Genomic Record Gene) is gene of a novel bioinformatically detected group of regulatory, non protein coding, RNA genes. The method by which VGR is detected is described hereinabove with reference to FIGS.

1-9.

[0127] VGR GENE encodes an RNA molecule, typically several hundred nucleotides long, designated VGR PRECURSOR RNA.

[0128] VGR PRECURSOR RNA folds spatially, as illustrated by VGR FOLDED PRECURSOR RNA, into a plurality of what is known in the art as "hairpin structures. The nucleotide sequence of VGR PRECURSOR RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, thereby causing formation of a plurality of "hairpin" structures, as is well known in the art.

[0129] VGR FOLDED PRECURSOR RNA is naturally processed by cellular enzymatic activity, into 3 separate hairpin shaped RNA segments, each corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1, designated VGAM1 FOLDED

PRECURSOR, VGAM2 FOLDED PRECURSOR and VGAM3 FOLDED PRECURSOR respectively.

[0130] The above mentioned VGAM precursors, are diced by DICER COMPLEX of FIG. 1, yielding short RNA segments of about 22 nucleotides in length, each corresponding to VGAM RNA of FIG. 1, designated VGAM1 RNA, VGAM2 RNA and VGAM3 RNA respectively.

[0131] VGAM1 RNA, VGAM2 RNA and VGAM3 RNA each bind complementarily to binding sites located in untranslated regions of respective host target, designated VGAM1-HOST TARGET RNA, VGAM2-HOST TARGET RNA and VGAM3-HOST TARGET RNA respectively. This binding inhibits translation of the respective target proteins designated VGAM1-HOST TARGET PROTEIN, VGAM2-HOST TARGET PROTEIN and VGAM3-HOST TARGET PROTEIN respectively.

[0132] The structure of VGAM genes comprised in a VGR GENE, and their mode of modulation of expression of their respective target genes is described hereinabove with reference to Fig. 1. The bioinformatic approach to detection of VGAM genes comprised in a VGR GENE is described hereinabove with reference to Figs. 1 through 9.

[0133] The present invention discloses 3283 novel viral genes of

the VGR group of genes, which have been detected bioinformatically, as described hereinbelow with reference to Fig. 1 through Fig. 9. Laboratory confirmation of three genes of the VGR group of genes is described hereinbelow with reference to Figs. 12A through 14B.

[0134] In summary, the current invention discloses a very large number of novel viral VGR genes, each of which encodes a plurality of VGAM genes, which in turn may modulate expression of a plurality of host target proteins.

[0135] Reference is now made to Fig. 10 which is a block diagram illustrating different utilities of genes of the novel group of genes of the present invention referred to here as VGAM genes and VGR genes.

[0136] The present invention discloses a first plurality of novel genes referred to here as VGAM genes, and a second plurality of operon-like genes referred to here as VGR genes, each of the VGR genes encoding a plurality of VGAM genes. The present invention further discloses a very large number of known target-genes, which are bound by, and the expression of which is modulated by each of the novel genes of the present invention. Published scientific data referenced by the present invention provides specific, substantial, and credible evidence that the abovementioned

tioned target genes modulated by novel genes of the present invention, are associated with various diseases. Specific novel genes of the present invention, target genes thereof and diseases associated therewith, are described hereinbelow with reference to Fig. 1 through Fig. 8. It is therefore appreciated that a function of VGAM genes and VGR genes of the present invention is modulation of expression of target genes related to known diseases, and that therefore utilities of novel genes of the present invention include diagnosis and treatment of the above-mentioned diseases. Fig. 10 describes various types of diagnostic and therapeutic utilities of novel genes of the present invention.

[0137] A utility of novel genes of the present invention is detection of VGAM genes and of VGR genes. It is appreciated that since VGAM genes and VGR genes modulate expression of disease related target genes, that detection of expression of VGAM genes in clinical scenarios associated with said diseases is a specific, substantial and credible utility. Diagnosis of novel genes of the present invention may preferably be implemented by RNA expression detection techniques, including but not limited to biochips, as is well known in the art. Diagnosis of expression of genes

of the present invention may be useful for research purposes, in order to further understand the connection between the novel genes of the present invention and the abovementioned related diseases, for disease diagnosis and prevention purposes, and for monitoring disease progress.

[0138] Another utility of novel genes of the present invention is anti-VGAM gene therapy, a mode of therapy which allows up regulation of a disease related target-gene of a novel VGAM gene of the present invention, by lowering levels of the novel VGAM gene which naturally inhibits expression of that target gene. This mode of therapy is particularly useful with respect to target genes which have been shown to be under-expressed in association with a specific disease. Anti-VGAM gene therapy is further discussed hereinbelow with reference to Figs. 11A and 11B.

[0139] A further utility of novel genes of the present invention is VGAM replacement therapy, a mode of therapy which achieves down regulation of a disease related target-gene of a novel VGAM gene of the present invention, by raising levels of the VGAM gene which naturally inhibits expression of that target gene. This mode of therapy is particularly useful with respect to target genes which have been

shown to be over-expressed in association with a specific disease. VGAM replacement therapy involves introduction of supplementary VGAM gene products into a cell, or stimulation of a cell to produce excess VGAM gene products. VGAM replacement therapy may preferably be achieved by transfecting cells with an artificial DNA molecule encoding a VGAM gene, which causes the cells to produce the VGAM gene product, as is well known in the art.

[0140] Yet a further utility of novel genes of the present invention is modified VGAM therapy. Disease conditions are likely to exist, in which a mutation in a binding site of a VGAM gene prevents natural VGAM gene to effectively bind inhibit a disease related target-gene, causing up regulation of that target gene, and thereby contributing to the disease pathology. In such conditions, a modified VGAM gene is designed which effectively binds the mutated VGAM binding site, i.e. is an effective anti-sense of the mutated VGAM binding site, and is introduced in disease effected cells. Modified VGAM therapy is preferably achieved by transfecting cells with an artificial DNA molecule encoding the modified VGAM gene, which causes the cells to produce the modified VGAM gene

product, as is well known in the art.

[0141] An additional utility of novel genes of the present invention is induced cellular differentiation therapy. An aspect of the present invention is finding genes which determine cellular differentiation, as described hereinabove with reference to Fig. 11. Induced cellular differentiation therapy comprises transfection of cell with such VGAM genes thereby determining their differentiation as desired. It is appreciated that this approach may be widely applicable, inter alia as a means for auto transplantation harvesting cells of one cell-type from a patient, modifying their differentiation as desired, and then transplanting them back into the patient. It is further appreciated that this approach may also be utilized to modify cell differentiation in vivo, by transfecting cells in a genetically diseased tissue with a cell-differentiation determining VGAM gene, thus stimulating these cells to differentiate appropriately.

[0142] Reference is now made to Figs. 11A and 11B, simplified diagrams which when taken together illustrate anti-VGAM gene therapy mentioned hereinabove with reference to Fig. 10. A utility of novel genes of the present invention is anti-VGAM gene therapy, a mode of therapy which allows up regulation of a disease related target-gene of a novel

VGAM gene of the present invention, by lowering levels of the novel VGAM gene which naturally inhibits expression of that target gene. Fig. 11A shows a normal VGAM gene, inhibiting translation of a target gene of VGAM gene, by binding to a BINDING SITE found in an untranslated region of TARGET RNA, as described hereinabove with reference to Fig. 1.

[0143] Fig. 11B shows an example of anti-VGAM gene therapy. ANTI-VGAM RNA is short artificial RNA molecule the sequence of which is an anti-sense of VGAM RNA. Anti-VGAM treatment comprises transfecting diseased cells with ANTI-VGAM RNA, or with a DNA encoding thereof. The ANTI-VGAM RNA binds the natural VGAM RNA, thereby preventing binding of natural VGAM RNA to its BINDING SITE. This prevents natural translation inhibition of TARGET RNA by VGAM RNA, thereby up regulating expression of TARGET PROTEIN.

[0144] It is appreciated that anti-VGAM gene therapy is particularly useful with respect to target genes which have been shown to be under-expressed in association with a specific disease.

[0145] Reference is now made to Fig. 12A which is an annotated sequence of an EST comprising a novel gene detected by

the gene detection system of the present invention. Fig. 12A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST72223. It is appreciated that the sequence of this EST comprises sequences of one known miRNA gene, identified as MIR98, and of one novel GAM gene, referred to here as GAM24, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0146] Reference is now made to Figs. 12B and 12C that are pictures of laboratory results, which when taken together demonstrate laboratory confirmation of expression of the bioinformatically detected novel gene of Fig. 12A. Reference is now made to Fig. 12B which is a Northern blot analysis of MIR-98 and EST72223 transcripts. MIR-98 and EST72223 were reacted with MIR-98 and GAM24 probes as indicated in the figure. It is appreciated that the probes of both MIR-98 and GAM24 reacted with EST72223, indicating that EST72223 contains the sequences of MIR-98 and of GAM24. It is further appreciated that the probe of GAM24 does not cross-react with MIR-98.

[0147] Reference is now made to Fig. 12C. A Northern blot analysis of EST72223 and MIR-98 transfections were per-

formed, subsequently marking RNA by the MIR-98 and GAM24 probes . Left, Northern reacted with MIR-98, Right, Northern reacted with GAM24. The molecular Sizes of EST72223, MIR-98 and GAM24 are indicated by arrows. Hela are control cells that have not been introduced to exogenous RNA. EST and MIR-98 Transfections are RNA obtained from Hela transfected with EST72223 and MIR-98, respectively. MIR-98 and EST are the transcripts used for the transfection experiment. The results indicate that EST72223, when transfected into Hela cells, is cut yielding known miRNA gene MIR-98 and novel miRNA gene GAM24.

[0148] Reference is now made to Fig. 12D, which is a Northern blot of a lysate experiment with MIR-98 and GAM24. Northern blot analysis of hairpins in EST72223 . Left, Northern reacted with predicted Mir-98 hairpin probe, Right, Northern reacted with predicted GAM24 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of Mir-98 and GAM24 are 80nt and 100nt, respectively as indicated by arrows. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2-EST incubated 4h with Hela lysate; 3-EST without lysate; 4-Mir transcript incubated 4h with Hela lysate; 5-Mir

transcript incubated overnight with Hela lysate; 6– Mir transcript without lysate; 7–RNA extracted from Hela cells following transfection with Mir transcript.

[0149] Technical methods used in experiments, the results of which are depicted in Figs. 12B, 12C and 12D are as follows:

[0150] *Transcript preparations:* Digoxigenin (DIG) labeled transcripts were prepared from EST72223 (TIGER), MIR98 and predicted precursor hairpins by using a DIG RNA labeling kit (Roche Molecular Biochemicals) according to the manufacturer's protocol. Briefly, PCR products with T7 promoter at the 5' end or T3 promoter at the 3' end were prepared from each DNA in order to use it as a template to prepare sense and antisense transcripts, respectively. MIR–98 was amplified using EST72223 as a template with T7miR98 forward primer:

5'–"TAATACGACTCACTATAGGGTGAGGTAGTAAGTTGTATTGTT–3" and T3miR98 reverse primer:

5'–AATTAACCCTCACTAAAGGGAAAGTAGTAAGTTGTATAGTT–3" EST72223 was amplified with T7–EST 72223 forward

primer: 5'–TAATACGACTCACTATAGGCCCTTATTAGAGGATTCTGCT–3" and T3–EST72223 reverse

primer: 5'–AATTAACCCTCACTAAAGGTTTTTTTTTCCTGAG

ACAGAGT-3" Bet-4 was amplified using EST72223 as a template with Bet-4 forward primer:

5"-GAGGCAGGAGAATTGCTTGA- 3" and T3-EST72223 reverse

primer: 5"-AATTAACCCTCACTAAAGGCCTGAGACAGAGTCTTGCTC-3" The PCR products were cleaned and used for DIG-labeled or unlabeled transcription reactions with the appropriate polymerase. For transfection experiments, CAP reaction was performed by using a mMessage mMachine kit (Ambion).

[0151] *Transfection procedure:* Transfection of Hela cells was performed by using TransMessenger reagent (Qiagen) according to the manufacture's protocol. Briefly, Hela cells were seeded to $1-2 \times 10^6$ cells per plate a day before transfection. Two μg RNA transcripts were mixed with 8 μl Enhancer in a final volume of 100 μl , mixed and incubated at room temperature for 5 min. 16 μl TransMessenger reagent was added to the RNA-Enhancer, mixed and incubated for additional 10 min. Cell plates were washed with sterile PBS twice and then incubated with the transfection mix diluted with 2.5 ml DMEM medium without serum. Cells were incubated with transfection mix for three hours under their normal growth condition (37°C and 5% CO₂)

before the transfection mix was removed and a fresh DMEM medium containing serum was added to the cells. Cells were left to grow 48 hours before harvesting.

[0152] *Target RNA cleavage assay:* Cap-labeled target RNAs were generated using mMessage mMachineTM (Ambion). Caped RNA transcripts were preincubated at 30⁰C for 15 min in supplemented Hela S100 obtained from Computer Cell Culture, Mos, Belgium. After addition of all components, final concentrations were 100mM target RNA, 1m M ATP, 0.2mM GTP, 10U/ml RNasin, 30µg/ml creatine kinase, 25mM creatine phosphate, and 50% S100 extract. Incubation was continued for 4 hours to overnight. Cleavage reaction was stopped by the addition of 8 volumes of proteinase K buffer (200Mm Tris-Hcl, pH 7.5, 25m M EDTA, 300mM NaCl, and 2% SDS). Proteinase K, dissolved in 50mM Tris-HCl, pH 8, 5m M CaCl₂, and 50% glycerol, was added to a final concentration of 0.6 mg/ml. Samples were subjected to phenol/chlorophorm extraction and kept frozen until analyzed by urea-TBE PAGE.

[0153] *Northern analysis:* RNAs were extracted from cells by using Tri-reagent according to the manufacturer's protocol. The RNAs were dissolved in water and heated to 65⁰C to disrupt any association of the 25nt RNA with larger RNA

molecules. RNA were placed on ice and incubated for 30 min with PEG (MW=8000) in a final concentration of 5% and NaCl in a final concentration of 0.5M to precipitate high molecular weight nucleic acid. The RNAs were centrifuged at 10,000xg for 10 min to pellet the high molecular weight nucleic acid. The supernatant containing the low molecular weight RNAs was collected and three volumes of ethanol was added. The RNAs were placed at -200C for at least two hours and then centrifuged at 10,000xg for 10 min. The pellets were dissolved in Urea-TBE buffer (1Xtbe, 7M urea) for further analysis by a Northern blot.

[0154] RNA samples were boiled for 5 min before loading on 15%-8% polyacrylamide (19:1) gels containing 7M urea and 1xTBE. Gels were run in 1xTBE at a constant voltage of 300V and then transferred into a nylon membrane. The membrane was exposed to 3min ultraviolet light to cross link the RNAs to the membrane. Hybridization was performed overnight with DIG-labeled probes at 420C. Membranes were washed twice with SSCx2 and 0.2% SDS for 10 min. at 420C and then washed twice with SSCx0.5 for 5 min at room temperature. The membrane was then developed by using a DIG luminescent detection kit (Roche) us-

ing anti DIG and CSPD reaction, according to the manufacture's protocol.

[0155] It is appreciated that the data presented in Figs. 12A, 12B, 12C and 12D, when taken together validate the function of the bioinformatic gene detection engine 100 of Fig. 2. Fig. 12A shows a novel GAM gene bioinformatically detected by the bioinformatic gene detection engine 100, and Figs. 12B, 12C and 12D show laboratory confirmation of the expression of this novel gene. This is in accord with the engine training and validation methodology described hereinabove with reference to Fig. 3.

[0156] Reference is now made to Fig. 13A which is an annotated sequence of an EST comprising a novel gene detected by the gene detection system of the present invention. Fig. 13A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST 7929020. It is appreciated that the sequence of this EST comprises sequences of two novel GAM genes, referred to here as GAM23 and GAM25, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0157] Reference is now made to Fig. 13B which presents pictures of laboratory results, that demonstrate laboratory

confirmation of expression of the bioinformatically detected novel gene of Fig. 13A. Northern blot analysis of hairpins in EST7929020. Left, Northern reacted with predicted GAM25 hairpin probe, Right, Northern reacted with predicted GAM23 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of GAM23 and GAM25 are 60nt, as indicated by arrow. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2- EST incubated 4h with Hela lysate ; 3- EST incubated overnight with Hela lysate; 4-EST without lysate; 5-GAM transcript; 6- GAM 22nt marker;7-GAM PCR probe; 8-RNA from control Hela cells; 9-RNA extracted from Hela cells following transfection with EST.

[0158] Reference is now made to Fig. 13C which is a picture of a Northern blot confirming Endogenous expression of bioinformatically detected gene GAM25 of Fig. 13A from in Hela cells. Northern was reacted with a predicted GAM25 hairpin probe. The molecular size of EST7929020 is indicated. The molecular sizes of GAM25 is 58nt, as indicated. A 19nt DNA oligo molecular marker is indicated. Endogenous expression of GAM25 in Hela total RNA fraction and in S-100 fraction is indicated by arrows. 1-GAM25 transcript; 2- GAM25 DNA oligo marker; 3-RNA

from control Hela cells; 4-RNA extracted from Hela cells following transfection with EST; 5- RNA extracted from S-100 Hela lysate.

[0159] Reference is now made to Fig. 14A which is an annotated sequence of an EST comprising a novel gene detected by the gene detection system of the present invention. Fig. 14A shows the nucleotide sequence of a known human non-protein coding EST (Expressed Sequence Tag), identified as EST 1388749. It is appreciated that the sequence of this EST comprises sequence of a novel GAM gene, referred to here as GAM26, detected by the bioinformatic gene detection system of the present invention, described hereinabove with reference to Fig. 2.

[0160] Reference is now made to Fig. 14B which is a picture of Northern blot analysis, confirming expression of novel bioinformatically detected gene GAM26, and natural processing thereof from EST1388749. Northern reacted with predicted GAM26 hairpin probe. The molecular size of EST is indicated by arrow. The molecular sizes of GAM26 is 130nt, as indicated by arrow. The 22nt molecular marker is indicated by arrow. 1-Hela lysate; 2-EST incubated 4h with Hela lysate; 3- EST incubated overnight with Hela lysate; 4-EST without lysate; 5-GAM transcript; 6- GAM

22nt marker; 7-GAM PCR probe.

[0161] Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2740(VGR2740) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0162] VGR2740 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2740 gene was detected is described hereinabove with reference to Figs. 1-9.

[0163] VGR2740 gene encodes VGR2740 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0164] VGR2740 precursor RNA folds spatially, forming VGR2740 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2740 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2740 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0165] VGR2740 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM15 precursor RNA and VGAM16 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0166] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM15 RNA and VGAM16 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0167] VGAM15 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM15 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM15 host target RNA into VGAM15 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0168] VGAM16 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM16 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM16 host target RNA into VGAM16 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0169] It is appreciated that a function of VGR2740 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2740 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2740 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2740 gene: VGAM15 host target protein and VGAM16 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM15 and VGAM16. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2741(VGR2741) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0170] VGR2741 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2741 gene was detected is described hereinabove with reference to Figs.

1-9.

[0171] VGR2741 gene encodes VGR2741 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0172] VGR2741 precursor RNA folds spatially, forming VGR2741 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2741 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2741 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0173] VGR2741 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM18 precursor RNA, VGAM19 precursor RNA, VGAM20 precursor RNA, VGAM21 precursor RNA, VGAM22 precursor RNA, VGAM23 precursor RNA, VGAM24 precursor RNA and VGAM25 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of

which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0174] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM18 RNA, VGAM19 RNA, VGAM20 RNA, VGAM21 RNA, VGAM22 RNA, VGAM23 RNA, VGAM24 RNA and VGAM25 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0175] VGAM18 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM18 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM18 host target RNA into VGAM18 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0176] VGAM19 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM19 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM19 host target RNA into VGAM19 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0177] VGAM20 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM20 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM20 host target RNA into VGAM20 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0178] VGAM21 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM21 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM21 host target RNA into VGAM21 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0179] VGAM22 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM22 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM22 host target RNA into VGAM22 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0180] VGAM23 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM23 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM23 host target RNA into VGAM23 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0181] VGAM24 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM24 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM24 host target RNA into

VGAM24 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0182] VGAM25 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM25 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM25 host target RNA into VGAM25 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0183] It is appreciated that a function of VGR2741 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2741 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2741 gene correlate with, and may be deduced from, the identity of the host target

genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2741 gene: VGAM18 host target protein, VGAM19 host target protein, VGAM20 host target protein, VGAM21 host target protein, VGAM22 host target protein, VGAM23 host target protein, VGAM24 host target protein and VGAM25 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM18, VGAM19, VGAM20, VGAM21, VGAM22, VGAM23, VGAM24 and VGAM25. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2742(VGR2742) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0184] VGR2742 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2742 gene was detected is described hereinabove with reference to Figs. 1-9.

- [0185] VGR2742 gene encodes VGR2742 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [0186] VGR2742 precursor RNA folds spatially, forming VGR2742 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2742 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2742 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [0187] VGR2742 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM26 precursor RNA, VGAM27 precursor RNA, VGAM28 precursor RNA, VGAM29 precursor RNA, VGAM30 precursor RNA, VGAM31 precursor RNA, VGAM32 precursor RNA and VGAM33 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA

segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0188] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM26 RNA, VGAM27 RNA, VGAM28 RNA, VGAM29 RNA, VGAM30 RNA, VGAM31 RNA, VGAM32 RNA and VGAM33 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0189] VGAM26 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM26 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM26 host target RNA into VGAM26 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0190] VGAM27 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM27 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM27 host target RNA into VGAM27 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0191] VGAM28 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM28 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM28 host target RNA into VGAM28 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0192] VGAM29 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM29 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM29 host target RNA into VGAM29 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0193] VGAM30 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM30 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM30 host target RNA into VGAM30 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0194] VGAM31 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM31 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM31 host target RNA into VGAM31 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0195] VGAM32 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM32 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM32 host target RNA into VGAM32 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0196] VGAM33 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM33 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM33 host target RNA into VGAM33 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0197] It is appreciated that a function of VGR2742 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2742 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2742 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in

the `operon-like` cluster of VGR2742 gene: VGAM26 host target protein, VGAM27 host target protein, VGAM28 host target protein, VGAM29 host target protein, VGAM30 host target protein, VGAM31 host target protein, VGAM32 host target protein and VGAM33 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM26, VGAM27, VGAM28, VGAM29, VGAM30, VGAM31, VGAM32 and VGAM33. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2743(VGR2743) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0198] VGR2743 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2743 gene was detected is described hereinabove with reference to Figs. 1-9.

[0199] VGR2743 gene encodes VGR2743 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0200] VGR2743 precursor RNA folds spatially, forming VGR2743 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2743 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2743 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0201] VGR2743 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM34 precursor RNA, VGAM35 precursor RNA, VGAM36 precursor RNA, VGAM37 precursor RNA, VGAM38 precursor RNA, VGAM39 precursor RNA, VGAM40 precursor RNA and VGAM41 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR

RNA of Fig. 1.

[0202] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM34 RNA, VGAM35 RNA, VGAM36 RNA, VGAM37 RNA, VGAM38 RNA, VGAM39 RNA, VGAM40 RNA and VGAM41 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0203] VGAM34 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM34 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM34 host target RNA into VGAM34 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0204] VGAM35 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM35 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM35 host target RNA into VGAM35 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0205] VGAM36 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM36 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM36 host target RNA into VGAM36 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0206] VGAM37 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM37 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM37 host target RNA into VGAM37 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0207] VGAM38 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM38 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM38 host target RNA into VGAM38 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0208] VGAM39 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM39 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM39 host target RNA into VGAM39 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0209] VGAM40 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM40 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM40 host target RNA into VGAM40 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0210] VGAM41 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM41 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM41 host target RNA into VGAM41 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0211] It is appreciated that a function of VGR2743 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2743 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2743 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2743 gene: VGAM34 host

target protein, VGAM35 host target protein, VGAM36 host target protein, VGAM37 host target protein, VGAM38 host target protein, VGAM39 host target protein, VGAM40 host target protein and VGAM41 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM34, VGAM35, VGAM36, VGAM37, VGAM38, VGAM39, VGAM40 and VGAM41. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2744(VGR2744) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0212] VGR2744 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2744 gene was detected is described hereinabove with reference to Figs. 1-9.

[0213] VGR2744 gene encodes VGR2744 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[0214] VGR2744 precursor RNA folds spatially, forming VGR2744 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2744 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2744 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0215] VGR2744 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM42 precursor RNA, VGAM43 precursor RNA, VGAM44 precursor RNA, VGAM45 precursor RNA, VGAM46 precursor RNA, VGAM47 precursor RNA, VGAM48 precursor RNA and VGAM49 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0216] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM42 RNA, VGAM43 RNA, VGAM44 RNA, VGAM45 RNA, VGAM46 RNA, VGAM47 RNA, VGAM48 RNA and VGAM49 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0217] VGAM42 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM42 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM42 host target RNA into VGAM42 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0218] VGAM43 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM43 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM43 host target RNA into VGAM43 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0219] VGAM44 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM44 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM44 host target RNA into VGAM44 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0220] VGAM45 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM45 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM45 host target RNA into VGAM45 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0221] VGAM46 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM46 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM46 host target RNA into VGAM46 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0222] VGAM47 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM47 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM47 host target RNA into VGAM47 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0223] VGAM48 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM48 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM48 host target RNA into VGAM48 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0224] VGAM49 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM49 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM49 host target RNA into VGAM49 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0225] It is appreciated that a function of VGR2744 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2744 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2744 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2744 gene: VGAM42 host target protein, VGAM43 host target protein, VGAM44 host

target protein, VGAM45 host target protein, VGAM46 host target protein, VGAM47 host target protein, VGAM48 host target protein and VGAM49 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM42, VGAM43, VGAM44, VGAM45, VGAM46, VGAM47, VGAM48 and VGAM49. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2745 (VGR2745) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0226] VGR2745 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2745 gene was detected is described hereinabove with reference to Figs. 1-9.

[0227] VGR2745 gene encodes VGR2745 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0228] VGR2745 precursor RNA folds spatially, forming VGR2745 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2745 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2745 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0229] VGR2745 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM50 precursor RNA, VGAM51 precursor RNA, VGAM52 precursor RNA, VGAM53 precursor RNA, VGAM54 precursor RNA, VGAM55 precursor RNA, VGAM56 precursor RNA and VGAM57 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0230] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM50 RNA, VGAM51 RNA, VGAM52 RNA, VGAM53 RNA, VGAM54 RNA, VGAM55 RNA, VGAM56 RNA and VGAM57 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0231] VGAM50 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM50 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM50 host target RNA into VGAM50 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0232] VGAM51 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM51 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM51 host target RNA into VGAM51 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0233] VGAM52 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM52 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM52 host target RNA into VGAM52 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0234] VGAM53 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM53 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM53 host target RNA into VGAM53 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0235] VGAM54 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM54 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM54 host target RNA into VGAM54 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0236] VGAM55 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM55 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM55 host target RNA into VGAM55 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0237] VGAM56 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM56 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM56 host target RNA into VGAM56 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0238] VGAM57 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM57 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM57 host target RNA into VGAM57 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0239] It is appreciated that a function of VGR2745 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2745 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2745 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2745 gene: VGAM50 host target protein, VGAM51 host target protein, VGAM52 host target protein, VGAM53 host target protein, VGAM54 host

target protein, VGAM55 host target protein, VGAM56 host target protein and VGAM57 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM50, VGAM51, VGAM52, VGAM53, VGAM54, VGAM55, VGAM56 and VGAM57. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2746 (VGR2746) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0240] VGR2746 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2746 gene was detected is described hereinabove with reference to Figs. 1-9.

[0241] VGR2746 gene encodes VGR2746 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0242] VGR2746 precursor RNA folds spatially, forming VGR2746

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2746 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2746 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0243] VGR2746 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM58 precursor RNA, VGAM59 precursor RNA, VGAM60 precursor RNA, VGAM61 precursor RNA, VGAM62 precursor RNA, VGAM63 precursor RNA, VGAM64 precursor RNA and VGAM65 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0244] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM58 RNA, VGAM59 RNA, VGAM60 RNA, VGAM61 RNA, VGAM62 RNA, VGAM63 RNA, VGAM64 RNA and VGAM65 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0245] VGAM58 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM58 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM58 host target RNA into VGAM58 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0246] VGAM59 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM59 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM59 host target RNA into VGAM59 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0247] VGAM60 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM60 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM60 host target RNA into VGAM60 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0248] VGAM61 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM61 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM61 host target RNA into VGAM61 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0249] VGAM62 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM62 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM62 host target RNA into VGAM62 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0250] VGAM63 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM63 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM63 host target RNA into VGAM63 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0251] VGAM64 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM64 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM64 host target RNA into VGAM64 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0252] VGAM65 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM65 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM65 host target RNA into VGAM65 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0253] It is appreciated that a function of VGR2746 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2746 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2746 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2746 gene: VGAM58 host target protein, VGAM59 host target protein, VGAM60 host target protein, VGAM61 host target protein, VGAM62 host target protein, VGAM63 host target protein, VGAM64 host

target protein and VGAM65 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM58, VGAM59, VGAM60, VGAM61, VGAM62, VGAM63, VGAM64 and VGAM65. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2747 (VGR2747) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0254] VGR2747 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2747 gene was detected is described hereinabove with reference to Figs. 1-9.

[0255] VGR2747 gene encodes VGR2747 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0256] VGR2747 precursor RNA folds spatially, forming VGR2747 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2747 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2747 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0257] VGR2747 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM66 precursor RNA, VGAM67 precursor RNA, VGAM68 precursor RNA, VGAM69 precursor RNA, VGAM70 precursor RNA, VGAM71 precursor RNA, VGAM72 precursor RNA and VGAM73 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0258] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM66

RNA, VGAM67 RNA, VGAM68 RNA, VGAM69 RNA, VGAM70 RNA, VGAM71 RNA, VGAM72 RNA and VGAM73 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0259] VGAM66 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM66 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM66 host target RNA into VGAM66 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0260] VGAM67 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM67 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM67 host target RNA into VGAM67 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0261] VGAM68 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM68 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM68 host target RNA into VGAM68 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0262] VGAM69 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM69 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM69 host target RNA into VGAM69 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0263] VGAM70 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM70 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM70 host target RNA into VGAM70 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0264] VGAM71 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM71 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM71 host target RNA into VGAM71 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0265] VGAM72 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM72 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM72 host target RNA into VGAM72 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0266] VGAM73 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM73 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM73 host target RNA into VGAM73 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0267] It is appreciated that a function of VGR2747 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2747 gene include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGR2747 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2747 gene: VGAM66 host target protein, VGAM67 host target protein, VGAM68 host target protein, VGAM69 host target protein, VGAM70 host target protein, VGAM71 host target protein, VGAM72 host target protein and VGAM73 host target protein, herein

schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM66, VGAM67, VGAM68, VGAM69, VGAM70, VGAM71, VGAM72 and VGAM73. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2748 (VGR2748) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0268] VGR2748 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2748 gene was detected is described hereinabove with reference to Figs. 1-9.

[0269] VGR2748 gene encodes VGR2748 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0270] VGR2748 precursor RNA folds spatially, forming VGR2748 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2748 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2748 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0271] VGR2748 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM76 precursor RNA and VGAM77 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0272] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM76 RNA and VGAM77 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0273] VGAM76 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM76 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM76 host target RNA into VGAM76 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0274] VGAM77 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM77 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM77 host target RNA into VGAM77 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0275] It is appreciated that a function of VGR2748 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2748 gene include diagnosis, prevention and treatment of viral infection by Murine Adenovirus A. Specific functions, and accordingly utilities, of VGR2748 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2748 gene: VGAM76 host target protein and VGAM77 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM76 and VGAM77. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2749(VGR2749) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0276] VGR2749 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2749 gene was detected is described hereinabove with reference to Figs. 1-9.

[0277] VGR2749 gene encodes VGR2749 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0278] VGR2749 precursor RNA folds spatially, forming VGR2749 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2749 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2749 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0279] VGR2749 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM78 precursor RNA, VGAM79 precursor RNA, VGAM80 precursor RNA, VGAM81 precursor RNA, VGAM82 precursor RNA, VGAM83 precursor RNA,

VGAM84 precursor RNA and VGAM85 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0280] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM78 RNA, VGAM79 RNA, VGAM80 RNA, VGAM81 RNA, VGAM82 RNA, VGAM83 RNA, VGAM84 RNA and VGAM85 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0281] VGAM78 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM78 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM78 host target RNA into

VGAM78 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0282] VGAM79 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM79 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM79 host target RNA into VGAM79 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0283] VGAM80 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM80 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM80 host target RNA into VGAM80 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0284] VGAM81 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM81 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM81 host target RNA into VGAM81 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0285] VGAM82 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM82 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM82 host target RNA into VGAM82 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0286] VGAM83 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM83 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM83 host target RNA into VGAM83 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0287] VGAM84 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM84 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM84 host target RNA into VGAM84 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0288] VGAM85 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM85 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM85 host target RNA into VGAM85 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0289] It is appreciated that a function of VGR2749 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2749 gene include diagnosis, prevention and treatment of viral infection by

Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGR2749 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2749 gene: VGAM78 host target protein, VGAM79 host target protein, VGAM80 host target protein, VGAM81 host target protein, VGAM82 host target protein, VGAM83 host target protein, VGAM84 host target protein and VGAM85 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM78, VGAM79, VGAM80, VGAM81, VGAM82, VGAM83, VGAM84 and VGAM85. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2750(VGR2750) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0290] VGR2750 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2750 gene was detected is described hereinabove with reference to Figs. 1-9.

[0291] VGR2750 gene encodes VGR2750 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0292] VGR2750 precursor RNA folds spatially, forming VGR2750 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2750 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2750 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0293] VGR2750 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM86 precursor RNA, VGAM87 precursor RNA, VGAM88 precursor RNA, VGAM89 precursor RNA, VGAM90 precursor RNA, VGAM91 precursor RNA, VGAM92 precursor RNA and VGAM93 precursor RNA,

herein schematically represented by VGAM1 FOLDED PRE-CURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0294] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM86 RNA, VGAM87 RNA, VGAM88 RNA, VGAM89 RNA, VGAM90 RNA, VGAM91 RNA, VGAM92 RNA and VGAM93 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0295] VGAM86 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM86 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM86 host target RNA into VGAM86 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0296] VGAM87 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM87 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM87 host target RNA into VGAM87 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0297] VGAM88 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM88 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM88 host target RNA into

VGAM88 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0298] VGAM89 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM89 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM89 host target RNA into VGAM89 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0299] VGAM90 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM90 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM90 host target RNA into VGAM90 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0300] VGAM91 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM91 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM91 host target RNA into VGAM91 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0301] VGAM92 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM92 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM92 host target RNA into VGAM92 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0302] VGAM93 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM93 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM93 host target RNA into VGAM93 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0303] It is appreciated that a function of VGR2750 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2750 gene include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and ac-

cordingly utilities, of VGR2750 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2750 gene: VGAM86 host target protein, VGAM87 host target protein, VGAM88 host target protein, VGAM89 host target protein, VGAM90 host target protein, VGAM91 host target protein, VGAM92 host target protein and VGAM93 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM86, VGAM87, VGAM88, VGAM89, VGAM90, VGAM91, VGAM92 and VGAM93. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2751(VGR2751) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0304] VGR2751 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2751 gene was

detected is described hereinabove with reference to Figs. 1–9.

[0305] VGR2751 gene encodes VGR2751 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0306] VGR2751 precursor RNA folds spatially, forming VGR2751 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2751 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2751 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0307] VGR2751 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM94 precursor RNA, VGAM95 precursor RNA, VGAM96 precursor RNA, VGAM97 precursor RNA, VGAM98 precursor RNA, VGAM99 precursor RNA, VGAM100 precursor RNA and VGAM101 precursor RNA, herein schematically represented by VGAM1 FOLDED PRE-

CURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0308] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM94 RNA, VGAM95 RNA, VGAM96 RNA, VGAM97 RNA, VGAM98 RNA, VGAM99 RNA, VGAM100 RNA and VGAM101 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0309] VGAM94 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM94 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM94 host target RNA into VGAM94 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0310] VGAM95 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM95 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM95 host target RNA into VGAM95 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0311] VGAM96 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM96 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM96 host target RNA into VGAM96 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0312] VGAM97 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM97 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM97 host target RNA into VGAM97 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0313] VGAM98 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM98 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM98 host target RNA into

VGAM98 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0314] VGAM99 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM99 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM99 host target RNA into VGAM99 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0315] VGAM100 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM100 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM100 host target RNA into VGAM100 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0316] VGAM101 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM101 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM101 host target RNA into VGAM101 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0317] It is appreciated that a function of VGR2751 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2751 gene include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGR2751 gene correlate with, and

may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2751 gene: VGAM94 host target protein, VGAM95 host target protein, VGAM96 host target protein, VGAM97 host target protein, VGAM98 host target protein, VGAM99 host target protein, VGAM100 host target protein and VGAM101 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM94, VGAM95, VGAM96, VGAM97, VGAM98, VGAM99, VGAM100 and VGAM101. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2752(VGR2752) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0318] VGR2752 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2752 gene was

detected is described hereinabove with reference to Figs. 1-9.

[0319] VGR2752 gene encodes VGR2752 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0320] VGR2752 precursor RNA folds spatially, forming VGR2752 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2752 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2752 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0321] VGR2752 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM102 precursor RNA, VGAM103 precursor RNA, VGAM104 precursor RNA and VGAM105 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin

shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0322] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM102 RNA, VGAM103 RNA, VGAM104 RNA and VGAM105 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0323] VGAM102 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM102 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM102 host target RNA into VGAM102 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0324] VGAM103 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM103 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM103 host target RNA into VGAM103 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0325] VGAM104 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM104 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM104 host target RNA into VGAM104 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0326] VGAM105 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM105 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM105 host target RNA into VGAM105 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0327] It is appreciated that a function of VGR2752 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2752 gene include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGR2752 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2752 gene: VGAM102 host target protein, VGAM103 host target protein, VGAM104 host target protein and VGAM105 host target

protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM102, VGAM103, VGAM104 and VGAM105. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2753(VGR2753) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0328] VGR2753 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2753 gene was detected is described hereinabove with reference to Figs. 1-9.

[0329] VGR2753 gene encodes VGR2753 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0330] VGR2753 precursor RNA folds spatially, forming VGR2753 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2753 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2753 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0331] VGR2753 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM106 precursor RNA, VGAM107 precursor RNA, VGAM108 precursor RNA and VGAM109 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0332] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM106 RNA, VGAM107 RNA, VGAM108 RNA and VGAM109 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to

VGAM RNA of Fig. 1.

[0333] VGAM106 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM106 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM106 host target RNA into VGAM106 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0334] VGAM107 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM107 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM107 host target RNA into VGAM107 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0335] VGAM108 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM108 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM108 host target RNA into VGAM108 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0336] VGAM109 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM109 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM109 host target RNA into

VGAM109 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0337] It is appreciated that a function of VGR2753 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2753 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2753 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2753 gene: VGAM106 host target protein, VGAM107 host target protein, VGAM108 host target protein and VGAM109 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM106, VGAM107, VGAM108 and VGAM109. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2754(VGR2754) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0338] VGR2754 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2754 gene was detected is described hereinabove with reference to Figs. 1-9.

[0339] VGR2754 gene encodes VGR2754 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0340] VGR2754 precursor RNA folds spatially, forming VGR2754 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2754 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2754 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0341] VGR2754 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM110 precursor RNA, VGAM111 precursor RNA, VGAM112 precursor RNA, VGAM113 precursor RNA, VGAM114 precursor RNA, VGAM115 precursor RNA, VGAM116 precursor RNA and VGAM117 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0342] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM110 RNA, VGAM111 RNA, VGAM112 RNA, VGAM113 RNA, VGAM114 RNA, VGAM115 RNA, VGAM116 RNA and VGAM117 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0343] VGAM110 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM110 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM110 host target RNA into VGAM110 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0344] VGAM111 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM111 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM111 host target RNA into VGAM111 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0345] VGAM112 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM112 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM112 host target RNA into VGAM112 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0346] VGAM113 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM113 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM113 host target RNA into VGAM113 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0347] VGAM114 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM114 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM114 host target RNA into VGAM114 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0348] VGAM115 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM115 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM115 host target RNA into VGAM115 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0349] VGAM116 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM116 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM116 host target RNA into VGAM116 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0350] VGAM117 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM117 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM117 host target RNA into VGAM117 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0351] It is appreciated that a function of VGR2754 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2754 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2754 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2754 gene: VGAM110 host target protein, VGAM111 host target protein, VGAM112 host target protein, VGAM113 host target protein, VGAM114 host target protein, VGAM115 host target protein, VGAM116 host target protein and VGAM117 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM110, VGAM111, VGAM112, VGAM113, VGAM114, VGAM115, VGAM116 and VGAM117. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2755(VGR2755)

viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0352] VGR2755 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2755 gene was detected is described hereinabove with reference to Figs. 1-9.

[0353] VGR2755 gene encodes VGR2755 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0354] VGR2755 precursor RNA folds spatially, forming VGR2755 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2755 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2755 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[0355] VGR2755 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM118 precursor RNA, VGAM119 precursor RNA, VGAM120 precursor RNA, VGAM121 precursor RNA, VGAM122 precursor RNA, VGAM123 precursor RNA, VGAM124 precursor RNA and VGAM125 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0356] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM118 RNA, VGAM119 RNA, VGAM120 RNA, VGAM121 RNA, VGAM122 RNA, VGAM123 RNA, VGAM124 RNA and VGAM125 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0357] VGAM118 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM118 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM118 host target RNA into VGAM118 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0358] VGAM119 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM119 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM119 host target RNA into VGAM119 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0359] VGAM120 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM120 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM120 host target RNA into VGAM120 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0360] VGAM121 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM121 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM121 host target RNA into VGAM121 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0361] VGAM122 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM122 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM122 host target RNA into VGAM122 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0362] VGAM123 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM123 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM123 host target RNA into VGAM123 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0363] VGAM124 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM124 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM124 host target RNA into VGAM124 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0364] VGAM125 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM125 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM125 host target RNA into VGAM125 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0365] It is appreciated that a function of VGR2755 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2755 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2755 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2755 gene: VGAM118 host target protein, VGAM119 host target protein, VGAM120 host target protein, VGAM121 host target protein, VGAM122 host target protein, VGAM123 host target protein, VGAM124 host target protein and VGAM125 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM118, VGAM119, VGAM120, VGAM121, VGAM122, VGAM123, VGAM124 and VGAM125. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene,

referred to here as Viral Genomic Record 2756(VGR2756) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0366] VGR2756 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2756 gene was detected is described hereinabove with reference to Figs. 1-9.

[0367] VGR2756 gene encodes VGR2756 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0368] VGR2756 precursor RNA folds spatially, forming VGR2756 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2756 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2756 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[0369] VGR2756 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM126 precursor RNA, VGAM127 precursor RNA, VGAM128 precursor RNA, VGAM129 precursor RNA, VGAM130 precursor RNA, VGAM131 precursor RNA, VGAM132 precursor RNA and VGAM133 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0370] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM126 RNA, VGAM127 RNA, VGAM128 RNA, VGAM129 RNA, VGAM130 RNA, VGAM131 RNA, VGAM132 RNA and VGAM133 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0371] VGAM126 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM126 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM126 host target RNA into VGAM126 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0372] VGAM127 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM127 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM127 host target RNA into VGAM127 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0373] VGAM128 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM128 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM128 host target RNA into VGAM128 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0374] VGAM129 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM129 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM129 host target RNA into VGAM129 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0375] VGAM130 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM130 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM130 host target RNA into VGAM130 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0376] VGAM131 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM131 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM131 host target RNA into VGAM131 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0377] VGAM132 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM132 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM132 host target RNA into VGAM132 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0378] VGAM133 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM133 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM133 host target RNA into VGAM133 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0379] It is appreciated that a function of VGR2756 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2756 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2756 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2756 gene: VGAM126 host target protein, VGAM127 host target protein, VGAM128 host target protein, VGAM129 host target protein, VGAM130 host target protein, VGAM131 host target protein, VGAM132 host target protein and VGAM133 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM126, VGAM127, VGAM128, VGAM129, VGAM130, VGAM131, VGAM132 and VGAM133. Fig. 9 further provides a conceptual description

of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2757(VGR2757) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0380] VGR2757 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2757 gene was detected is described hereinabove with reference to Figs. 1-9.

[0381] VGR2757 gene encodes VGR2757 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0382] VGR2757 precursor RNA folds spatially, forming VGR2757 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2757 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2757 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0383] VGR2757 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM134 precursor RNA, VGAM135 precursor RNA, VGAM136 precursor RNA, VGAM137 precursor RNA, VGAM138 precursor RNA, VGAM139 precursor RNA, VGAM140 precursor RNA and VGAM141 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0384] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM134 RNA, VGAM135 RNA, VGAM136 RNA, VGAM137 RNA, VGAM138 RNA, VGAM139 RNA, VGAM140 RNA and VGAM141 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0385] VGAM134 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM134 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM134 host target RNA into VGAM134 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0386] VGAM135 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM135 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM135 host target RNA into VGAM135 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0387] VGAM136 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM136 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM136 host target RNA into VGAM136 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0388] VGAM137 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM137 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM137 host target RNA into VGAM137 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0389] VGAM138 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM138 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM138 host target RNA into VGAM138 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0390] VGAM139 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM139 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM139 host target RNA into VGAM139 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0391] VGAM140 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM140 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM140 host target RNA into VGAM140 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0392] VGAM141 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM141 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM141 host target RNA into

VGAM141 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0393] It is appreciated that a function of VGR2757 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2757 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2757 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2757 gene: VGAM134 host target protein, VGAM135 host target protein, VGAM136 host target protein, VGAM137 host target protein, VGAM138 host target protein, VGAM139 host target protein, VGAM140 host target protein and VGAM141 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM134, VGAM135, VGAM136, VGAM137, VGAM138, VGAM139, VGAM140 and

VGAM141.Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2758(VGR2758) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0394] VGR2758 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2758 gene was detected is described hereinabove with reference to Figs. 1-9.

[0395] VGR2758 gene encodes VGR2758 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0396] VGR2758 precursor RNA folds spatially, forming VGR2758 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2758 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2758 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0397] VGR2758 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM142 precursor RNA, VGAM143 precursor RNA, VGAM144 precursor RNA, VGAM145 precursor RNA, VGAM146 precursor RNA, VGAM147 precursor RNA, VGAM148 precursor RNA and VGAM149 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0398] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM142 RNA, VGAM143 RNA, VGAM144 RNA, VGAM145 RNA, VGAM146 RNA, VGAM147 RNA, VGAM148 RNA and VGAM149 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0399] VGAM142 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM142 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM142 host target RNA into VGAM142 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0400] VGAM143 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM143 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM143 host target RNA into VGAM143 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0401] VGAM144 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM144 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM144 host target RNA into VGAM144 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0402] VGAM145 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM145 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM145 host target RNA into VGAM145 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0403] VGAM146 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM146 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM146 host target RNA into VGAM146 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0404] VGAM147 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM147 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM147 host target RNA into

VGAM147 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0405] VGAM148 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM148 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM148 host target RNA into VGAM148 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0406] VGAM149 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM149 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM149 host target RNA into VGAM149 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0407] It is appreciated that a function of VGR2758 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2758 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2758 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2758 gene: VGAM142 host target protein, VGAM143 host target protein, VGAM144 host target protein, VGAM145 host target protein, VGAM146 host target protein, VGAM147 host target protein, VGAM148 host target protein and VGAM149 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM142, VGAM143, VGAM144,

VGAM145, VGAM146, VGAM147, VGAM148 and VGAM149. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2759(VGR2759) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0408] VGR2759 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2759 gene was detected is described hereinabove with reference to Figs. 1-9.

[0409] VGR2759 gene encodes VGR2759 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0410] VGR2759 precursor RNA folds spatially, forming VGR2759 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2759 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2759 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0411] VGR2759 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM150 precursor RNA, VGAM151 precursor RNA, VGAM152 precursor RNA, VGAM153 precursor RNA, VGAM154 precursor RNA, VGAM155 precursor RNA, VGAM156 precursor RNA and VGAM157 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0412] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM150 RNA, VGAM151 RNA, VGAM152 RNA, VGAM153 RNA, VGAM154 RNA, VGAM155 RNA, VGAM156 RNA and VGAM157 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[0413] VGAM150 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM150 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM150 host target RNA into VGAM150 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0414] VGAM151 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM151 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM151 host target RNA into VGAM151 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0415] VGAM152 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM152 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM152 host target RNA into VGAM152 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0416] VGAM153 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM153 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM153 host target RNA into

VGAM153 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0417] VGAM154 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM154 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM154 host target RNA into VGAM154 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0418] VGAM155 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM155 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM155 host target RNA into VGAM155 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0419] VGAM156 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM156 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM156 host target RNA into VGAM156 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0420] VGAM157 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM157 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM157 host target RNA into VGAM157 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0421] It is appreciated that a function of VGR2759 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2759 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2759 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2759 gene: VGAM150 host target protein, VGAM151 host target protein, VGAM152 host target protein, VGAM153 host target protein, VGAM154 host target protein, VGAM155 host target protein, VGAM156 host target protein and VGAM157 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove

with reference to VGAM150, VGAM151, VGAM152, VGAM153, VGAM154, VGAM155, VGAM156 and VGAM157. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2760 (VGR2760) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0422] VGR2760 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2760 gene was detected is described hereinabove with reference to Figs. 1-9.

[0423] VGR2760 gene encodes VGR2760 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0424] VGR2760 precursor RNA folds spatially, forming VGR2760 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2760 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2760 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0425] VGR2760 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM158 precursor RNA, VGAM159 precursor RNA, VGAM160 precursor RNA, VGAM161 precursor RNA, VGAM162 precursor RNA, VGAM163 precursor RNA, VGAM164 precursor RNA and VGAM165 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0426] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM158 RNA, VGAM159 RNA, VGAM160 RNA, VGAM161 RNA, VGAM162 RNA, VGAM163 RNA, VGAM164 RNA and VGAM165 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0427] VGAM158 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM158 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM158 host target RNA into VGAM158 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0428] VGAM159 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM159 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM159 host target RNA into

VGAM159 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0429] VGAM160 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM160 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM160 host target RNA into VGAM160 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0430] VGAM161 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM161 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM161 host target RNA into VGAM161 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0431] VGAM162 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM162 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM162 host target RNA into VGAM162 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0432] VGAM163 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM163 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM163 host target RNA into VGAM163 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0433] VGAM164 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM164 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM164 host target RNA into VGAM164 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0434] VGAM165 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM165 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM165 host target RNA into VGAM165 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0435] It is appreciated that a function of VGR2760 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2760 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2760 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2760 gene: VGAM158 host target protein, VGAM159 host target protein, VGAM160 host target protein, VGAM161 host target protein, VGAM162 host target protein, VGAM163 host target protein, VGAM164 host target protein and VGAM165 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM158, VGAM159, VGAM160, VGAM161, VGAM162, VGAM163, VGAM164 and VGAM165. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2761 (VGR2761) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0436] VGR2761 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2761 gene was detected is described hereinabove with reference to Figs. 1-9.

[0437] VGR2761 gene encodes VGR2761 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0438] VGR2761 precursor RNA folds spatially, forming VGR2761 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2761 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2761 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0439] VGR2761 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM166 precursor RNA, VGAM167 precursor RNA, VGAM168 precursor RNA, VGAM169 precursor RNA, VGAM170 precursor RNA, VGAM171 precursor RNA, VGAM172 precursor RNA and VGAM173 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0440] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM166 RNA, VGAM167 RNA, VGAM168 RNA, VGAM169 RNA, VGAM170 RNA, VGAM171 RNA, VGAM172 RNA and

VGAM173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0441] VGAM166 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM166 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM166 host target RNA into VGAM166 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0442] VGAM167 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM167 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM167 host target RNA into VGAM167 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0443] VGAM168 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM168 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM168 host target RNA into VGAM168 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0444] VGAM169 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM169 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM169 host target RNA into VGAM169 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0445] VGAM170 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM170 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM170 host target RNA into VGAM170 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0446] VGAM171 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM171 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM171 host target RNA into VGAM171 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0447] VGAM172 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM172 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM172 host target RNA into VGAM172 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0448] VGAM173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM173 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM173 host target RNA into VGAM173 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0449] It is appreciated that a function of VGR2761 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2761 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2761 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2761 gene: VGAM166 host target protein, VGAM167 host target protein, VGAM168 host target protein, VGAM169 host target protein, VGAM170 host target protein, VGAM171 host target protein, VGAM172 host target protein and VGAM173 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM166, VGAM167, VGAM168, VGAM169, VGAM170, VGAM171, VGAM172 and VGAM173. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2762 (VGR2762) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0450] VGR2762 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2762 gene was detected is described hereinabove with reference to Figs. 1-9.

[0451] VGR2762 gene encodes VGR2762 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0452] VGR2762 precursor RNA folds spatially, forming VGR2762 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2762 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2762 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0453] VGR2762 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM174 precursor RNA, VGAM175 precursor RNA, VGAM176 precursor RNA, VGAM177 precursor RNA, VGAM178 precursor RNA, VGAM179 precursor RNA, VGAM180 precursor RNA and VGAM181 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0454] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM174 RNA, VGAM175 RNA, VGAM176 RNA, VGAM177 RNA,

VGAM178 RNA, VGAM179 RNA, VGAM180 RNA and VGAM181 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0455] VGAM174 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM174 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM174 host target RNA into VGAM174 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0456] VGAM175 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM175 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM175 host target RNA into VGAM175 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0457] VGAM176 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM176 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM176 host target RNA into VGAM176 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0458] VGAM177 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM177 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM177 host target RNA into VGAM177 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0459] VGAM178 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM178 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM178 host target RNA into VGAM178 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0460] VGAM179 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM179 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM179 host target RNA into VGAM179 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0461] VGAM180 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM180 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM180 host target RNA into VGAM180 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0462] VGAM181 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM181 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM181 host target RNA into VGAM181 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0463] It is appreciated that a function of VGR2762 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2762 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2762 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2762 gene: VGAM174 host target protein, VGAM175 host target protein, VGAM176 host target protein, VGAM177 host target protein, VGAM178 host target protein, VGAM179 host target protein, VGAM180 host target protein and VGAM181 host target protein, herein

schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM174, VGAM175, VGAM176, VGAM177, VGAM178, VGAM179, VGAM180 and VGAM181. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2763 (VGR2763) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0464] VGR2763 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2763 gene was detected is described hereinabove with reference to Figs. 1-9.

[0465] VGR2763 gene encodes VGR2763 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0466] VGR2763 precursor RNA folds spatially, forming VGR2763 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2763 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2763 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0467] VGR2763 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM182 precursor RNA, VGAM183 precursor RNA, VGAM184 precursor RNA, VGAM185 precursor RNA, VGAM186 precursor RNA, VGAM187 precursor RNA, VGAM188 precursor RNA and VGAM189 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0468] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM182

RNA, VGAM183 RNA, VGAM184 RNA, VGAM185 RNA, VGAM186 RNA, VGAM187 RNA, VGAM188 RNA and VGAM189 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0469] VGAM182 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM182 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM182 host target RNA into VGAM182 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0470] VGAM183 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM183 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM183 host target RNA into VGAM183 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0471] VGAM184 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM184 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM184 host target RNA into VGAM184 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0472] VGAM185 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM185 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM185 host target RNA into VGAM185 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0473] VGAM186 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM186 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM186 host target RNA into VGAM186 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0474] VGAM187 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM187 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM187 host target RNA into VGAM187 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0475] VGAM188 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM188 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM188 host target RNA into VGAM188 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0476] VGAM189 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM189 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM189 host target RNA into VGAM189 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0477] It is appreciated that a function of VGR2763 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2763 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2763 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2763 gene: VGAM182 host target protein, VGAM183 host target protein, VGAM184 host target protein, VGAM185 host target protein, VGAM186 host target protein, VGAM187 host target protein, VGAM188 host target

protein and VGAM189 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM182, VGAM183, VGAM184, VGAM185, VGAM186, VGAM187, VGAM188 and VGAM189. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2764(VGR2764) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0478] VGR2764 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2764 gene was detected is described hereinabove with reference to Figs. 1-9.

[0479] VGR2764 gene encodes VGR2764 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0480] VGR2764 precursor RNA folds spatially, forming VGR2764

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2764 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2764 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0481] VGR2764 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM190 precursor RNA, VGAM191 precursor RNA, VGAM192 precursor RNA, VGAM193 precursor RNA, VGAM194 precursor RNA, VGAM195 precursor RNA, VGAM196 precursor RNA and VGAM197 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0482] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM190 RNA, VGAM191 RNA, VGAM192 RNA, VGAM193 RNA, VGAM194 RNA, VGAM195 RNA, VGAM196 RNA and VGAM197 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0483] VGAM190 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM190 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM190 host target RNA into VGAM190 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0484] VGAM191 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM191 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM191 host target RNA into VGAM191 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0485] VGAM192 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM192 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM192 host target RNA into VGAM192 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0486] VGAM193 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM193 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM193 host target RNA into VGAM193 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0487] VGAM194 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM194 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM194 host target RNA into VGAM194 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0488] VGAM195 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM195 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM195 host target RNA into VGAM195 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0489] VGAM196 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM196 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM196 host target RNA into VGAM196 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0490] VGAM197 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM197 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM197 host target RNA into VGAM197 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0491] It is appreciated that a function of VGR2764 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2764 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2764 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2764 gene: VGAM190 host target protein, VGAM191 host target protein, VGAM192 host target protein, VGAM193 host target protein, VGAM194 host target pro-

tein, VGAM195 host target protein, VGAM196 host target protein and VGAM197 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM190, VGAM191, VGAM192, VGAM193, VGAM194, VGAM195, VGAM196 and VGAM197. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2765 (VGR2765) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0492] VGR2765 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2765 gene was detected is described hereinabove with reference to Figs. 1-9.

[0493] VGR2765 gene encodes VGR2765 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0494] VGR2765 precursor RNA folds spatially, forming VGR2765 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2765 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2765 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0495] VGR2765 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM198 precursor RNA, VGAM199 precursor RNA, VGAM200 precursor RNA, VGAM201 precursor RNA, VGAM202 precursor RNA, VGAM203 precursor RNA, VGAM204 precursor RNA and VGAM205 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0496] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM198 RNA, VGAM199 RNA, VGAM200 RNA, VGAM201 RNA, VGAM202 RNA, VGAM203 RNA, VGAM204 RNA and VGAM205 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0497] VGAM198 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM198 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM198 host target RNA into VGAM198 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0498] VGAM199 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM199 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM199 host target RNA into VGAM199 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0499] VGAM200 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM200 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM200 host target RNA into VGAM200 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0500] VGAM201 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM201 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM201 host target RNA into VGAM201 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0501] VGAM202 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM202 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM202 host target RNA into VGAM202 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0502] VGAM203 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM203 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM203 host target RNA into VGAM203 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0503] VGAM204 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM204 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM204 host target RNA into VGAM204 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0504] VGAM205 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM205 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM205 host target RNA into VGAM205 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0505] It is appreciated that a function of VGR2765 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2765 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2765 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2765 gene: VGAM198 host target protein, VGAM199 host target protein, VGAM200 host target protein,

VGAM201 host target protein, VGAM202 host target protein, VGAM203 host target protein, VGAM204 host target protein and VGAM205 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM198, VGAM199, VGAM200, VGAM201, VGAM202, VGAM203, VGAM204 and VGAM205. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2766(VGR2766) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0506] VGR2766 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2766 gene was detected is described hereinabove with reference to Figs. 1-9.

[0507] VGR2766 gene encodes VGR2766 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[0508] VGR2766 precursor RNA folds spatially, forming VGR2766 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2766 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2766 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0509] VGR2766 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM206 precursor RNA, VGAM207 precursor RNA, VGAM208 precursor RNA, VGAM209 precursor RNA and VGAM210 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0510] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM206 RNA, VGAM207 RNA, VGAM208 RNA, VGAM209 RNA and VGAM210 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0511] VGAM206 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM206 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM206 host target RNA into VGAM206 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0512] VGAM207 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM207 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM207 host target RNA into VGAM207 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0513] VGAM208 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM208 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM208 host target RNA into VGAM208 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0514] VGAM209 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM209 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM209 host target RNA into VGAM209 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0515] VGAM210 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM210 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM210 host target RNA into VGAM210 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0516] It is appreciated that a function of VGR2766 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2766 gene include

diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2766 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2766 gene: VGAM206 host target protein, VGAM207 host target protein, VGAM208 host target protein, VGAM209 host target protein and VGAM210 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM206, VGAM207, VGAM208, VGAM209 and VGAM210. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2767(VGR2767) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0517] VGR2767 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2767 gene was detected is described hereinabove with reference to Figs. 1-9.

[0518] VGR2767 gene encodes VGR2767 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0519] VGR2767 precursor RNA folds spatially, forming VGR2767 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2767 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2767 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0520] VGR2767 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM211 precursor RNA, VGAM212 precursor RNA and VGAM213 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0521] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM211 RNA, VGAM212 RNA and VGAM213 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0522] VGAM211 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM211 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM211 host target RNA into VGAM211 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0523] VGAM212 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM212 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM212 host target RNA into VGAM212 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0524] VGAM213 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM213 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM213 host target RNA into VGAM213 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0525] It is appreciated that a function of VGR2767 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2767 gene include diagnosis, prevention and treatment of viral infection by Simian Virus 40. Specific functions, and accordingly utilities, of VGR2767 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2767 gene: VGAM211 host target protein, VGAM212 host target protein and VGAM213 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM211, VGAM212 and VGAM213. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2768(VGR2768) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0526] VGR2768 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2768 gene was detected is described hereinabove with reference to Figs. 1–9.

[0527] VGR2768 gene encodes VGR2768 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0528] VGR2768 precursor RNA folds spatially, forming VGR2768 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2768 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2768 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[0529] VGR2768 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM214 precursor RNA and VGAM215 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0530] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM214 RNA and VGAM215 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0531] VGAM214 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM214 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM214 host target RNA into VGAM214 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0532] VGAM215 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM215 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM215 host target RNA into VGAM215 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0533] It is appreciated that a function of VGR2768 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2768 gene include diagnosis, prevention and treatment of viral infection by Autographa Californica Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2768 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2768 gene: VGAM214 host target protein and VGAM215 host target protein, herein schematically represented by VGAM1 HOST

TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN.

The function of these host target genes is elaborated hereinabove with reference to VGAM214 and

VGAM215. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2769 (VGR2769) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0534] VGR2769 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2769 gene was detected is described hereinabove with reference to Figs. 1-9.

[0535] VGR2769 gene encodes VGR2769 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0536] VGR2769 precursor RNA folds spatially, forming VGR2769 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2769 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2769 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0537] VGR2769 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM216 precursor RNA and VGAM217 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0538] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM216 RNA and VGAM217 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0539] VGAM216 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM216 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM216 host target RNA into VGAM216 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0540] VGAM217 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM217 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM217 host target RNA into VGAM217 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0541] It is appreciated that a function of VGR2769 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2769 gene include diagnosis, prevention and treatment of viral infection by Avian Leukosis Virus. Specific functions, and accordingly utilities, of VGR2769 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2769 gene: VGAM216 host target protein and VGAM217 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM216 and VGAM217. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2770(VGR2770) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0542] VGR2770 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2770 gene was detected is described hereinabove with reference to Figs. 1-9.

[0543] VGR2770 gene encodes VGR2770 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0544] VGR2770 precursor RNA folds spatially, forming VGR2770 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2770 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2770 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0545] VGR2770 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM218 precursor RNA and VGAM219 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0546] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM218 RNA and VGAM219 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0547] VGAM218 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM218 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM218 host target RNA into VGAM218 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0548] VGAM219 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM219 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM219 host target RNA into VGAM219 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0549] It is appreciated that a function of VGR2770 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2770 gene include diagnosis, prevention and treatment of viral infection by Bovine Leukemia Virus. Specific functions, and accordingly utilities, of VGR2770 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2770 gene: VGAM218 host target protein and VGAM219 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove

with reference to VGAM218 and VGAM219. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2771 (VGR2771) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0550] VGR2771 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2771 gene was detected is described hereinabove with reference to Figs. 1-9.

[0551] VGR2771 gene encodes VGR2771 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0552] VGR2771 precursor RNA folds spatially, forming VGR2771 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2771 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2771 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0553] VGR2771 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM220 precursor RNA, VGAM221 precursor RNA, VGAM222 precursor RNA, VGAM223 precursor RNA, VGAM224 precursor RNA, VGAM225 precursor RNA, VGAM226 precursor RNA and VGAM227 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0554] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM220 RNA, VGAM221 RNA, VGAM222 RNA, VGAM223 RNA, VGAM224 RNA, VGAM225 RNA, VGAM226 RNA and VGAM227 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0555] VGAM220 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM220 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM220 host target RNA into VGAM220 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0556] VGAM221 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM221 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM221 host target RNA into VGAM221 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0557] VGAM222 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM222 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM222 host target RNA into VGAM222 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0558] VGAM223 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM223 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM223 host target RNA into VGAM223 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0559] VGAM224 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM224 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM224 host target RNA into VGAM224 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0560] VGAM225 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM225 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM225 host target RNA into

VGAM225 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0561] VGAM226 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM226 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM226 host target RNA into VGAM226 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0562] VGAM227 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM227 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM227 host target RNA into VGAM227 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0563] It is appreciated that a function of VGR2771 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2771 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2771 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2771 gene: VGAM220 host target protein, VGAM221 host target protein, VGAM222 host target protein, VGAM223 host target protein, VGAM224 host target protein, VGAM225 host target protein, VGAM226 host target protein and VGAM227 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM220, VGAM221, VGAM222, VGAM223, VGAM224, VGAM225,

VGAM226 and VGAM227. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2772 (VGR2772) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0564] VGR2772 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2772 gene was detected is described hereinabove with reference to Figs. 1-9.

[0565] VGR2772 gene encodes VGR2772 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0566] VGR2772 precursor RNA folds spatially, forming VGR2772 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2772 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2772 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0567] VGR2772 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM228 precursor RNA, VGAM229 precursor RNA, VGAM230 precursor RNA, VGAM231 precursor RNA, VGAM232 precursor RNA, VGAM233 precursor RNA, VGAM234 precursor RNA and VGAM235 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0568] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM228 RNA, VGAM229 RNA, VGAM230 RNA, VGAM231 RNA, VGAM232 RNA, VGAM233 RNA, VGAM234 RNA and VGAM235 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0569] VGAM228 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM228 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM228 host target RNA into VGAM228 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0570] VGAM229 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM229 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM229 host target RNA into VGAM229 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0571] VGAM230 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM230 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM230 host target RNA into VGAM230 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0572] VGAM231 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM231 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM231 host target RNA into VGAM231 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0573] VGAM232 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM232 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM232 host target RNA into VGAM232 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0574] VGAM233 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM233 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM233 host target RNA into

VGAM233 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0575] VGAM234 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM234 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM234 host target RNA into VGAM234 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0576] VGAM235 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM235 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM235 host target RNA into VGAM235 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0577] It is appreciated that a function of VGR2772 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2772 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2772 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2772 gene: VGAM228 host target protein, VGAM229 host target protein, VGAM230 host target protein, VGAM231 host target protein, VGAM232 host target protein, VGAM233 host target protein, VGAM234 host target protein and VGAM235 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM228, VGAM229, VGAM230, VGAM231, VGAM232, VGAM233,

VGAM234 and VGAM235. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2773 (VGR2773) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0578] VGR2773 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2773 gene was detected is described hereinabove with reference to Figs. 1-9.

[0579] VGR2773 gene encodes VGR2773 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0580] VGR2773 precursor RNA folds spatially, forming VGR2773 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2773 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2773 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0581] VGR2773 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM236 precursor RNA, VGAM237 precursor RNA, VGAM238 precursor RNA, VGAM239 precursor RNA, VGAM240 precursor RNA, VGAM241 precursor RNA, VGAM242 precursor RNA and VGAM243 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0582] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM236 RNA, VGAM237 RNA, VGAM238 RNA, VGAM239 RNA, VGAM240 RNA, VGAM241 RNA, VGAM242 RNA and VGAM243 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0583] VGAM236 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM236 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM236 host target RNA into VGAM236 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0584] VGAM237 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM237 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM237 host target RNA into VGAM237 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0585] VGAM238 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM238 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM238 host target RNA into VGAM238 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0586] VGAM239 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM239 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM239 host target RNA into VGAM239 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0587] VGAM240 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM240 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM240 host target RNA into VGAM240 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0588] VGAM241 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM241 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM241 host target RNA into

VGAM241 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0589] VGAM242 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM242 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM242 host target RNA into VGAM242 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0590] VGAM243 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM243 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM243 host target RNA into VGAM243 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0591] It is appreciated that a function of VGR2773 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2773 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2773 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2773 gene: VGAM236 host target protein, VGAM237 host target protein, VGAM238 host target protein, VGAM239 host target protein, VGAM240 host target protein, VGAM241 host target protein, VGAM242 host target protein and VGAM243 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM236, VGAM237, VGAM238, VGAM239, VGAM240, VGAM241,

VGAM242 and VGAM243. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2774 (VGR2774) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0592] VGR2774 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2774 gene was detected is described hereinabove with reference to Figs. 1-9.

[0593] VGR2774 gene encodes VGR2774 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0594] VGR2774 precursor RNA folds spatially, forming VGR2774 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2774 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2774 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0595] VGR2774 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM244 precursor RNA, VGAM245 precursor RNA, VGAM246 precursor RNA, VGAM247 precursor RNA, VGAM248 precursor RNA, VGAM249 precursor RNA, VGAM250 precursor RNA and VGAM251 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0596] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM244 RNA, VGAM245 RNA, VGAM246 RNA, VGAM247 RNA, VGAM248 RNA, VGAM249 RNA, VGAM250 RNA and VGAM251 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0597] VGAM244 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM244 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM244 host target RNA into VGAM244 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0598] VGAM245 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM245 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM245 host target RNA into VGAM245 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0599] VGAM246 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM246 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM246 host target RNA into VGAM246 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0600] VGAM247 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM247 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM247 host target RNA into VGAM247 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0601] VGAM248 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM248 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM248 host target RNA into VGAM248 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0602] VGAM249 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM249 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM249 host target RNA into

VGAM249 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0603] VGAM250 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM250 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM250 host target RNA into VGAM250 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0604] VGAM251 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM251 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM251 host target RNA into VGAM251 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0605] It is appreciated that a function of VGR2774 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2774 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2774 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2774 gene: VGAM244 host target protein, VGAM245 host target protein, VGAM246 host target protein, VGAM247 host target protein, VGAM248 host target protein, VGAM249 host target protein, VGAM250 host target protein and VGAM251 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM244, VGAM245, VGAM246, VGAM247, VGAM248, VGAM249,

VGAM250 and VGAM251. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2775 (VGR2775) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0606] VGR2775 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2775 gene was detected is described hereinabove with reference to Figs. 1-9.

[0607] VGR2775 gene encodes VGR2775 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0608] VGR2775 precursor RNA folds spatially, forming VGR2775 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2775 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2775 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0609] VGR2775 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM252 precursor RNA, VGAM253 precursor RNA, VGAM254 precursor RNA, VGAM255 precursor RNA, VGAM256 precursor RNA, VGAM257 precursor RNA, VGAM258 precursor RNA and VGAM259 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0610] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM252 RNA, VGAM253 RNA, VGAM254 RNA, VGAM255 RNA, VGAM256 RNA, VGAM257 RNA, VGAM258 RNA and VGAM259 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0611] VGAM252 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM252 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM252 host target RNA into VGAM252 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0612] VGAM253 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM253 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM253 host target RNA into VGAM253 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0613] VGAM254 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM254 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM254 host target RNA into VGAM254 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0614] VGAM255 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM255 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM255 host target RNA into VGAM255 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0615] VGAM256 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM256 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM256 host target RNA into VGAM256 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0616] VGAM257 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM257 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM257 host target RNA into

VGAM257 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0617] VGAM258 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM258 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM258 host target RNA into VGAM258 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0618] VGAM259 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM259 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM259 host target RNA into VGAM259 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0619] It is appreciated that a function of VGR2775 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2775 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2775 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2775 gene: VGAM252 host target protein, VGAM253 host target protein, VGAM254 host target protein, VGAM255 host target protein, VGAM256 host target protein, VGAM257 host target protein, VGAM258 host target protein and VGAM259 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM252, VGAM253, VGAM254, VGAM255, VGAM256, VGAM257,

VGAM258 and VGAM259. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2776 (VGR2776) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0620] VGR2776 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2776 gene was detected is described hereinabove with reference to Figs. 1-9.

[0621] VGR2776 gene encodes VGR2776 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0622] VGR2776 precursor RNA folds spatially, forming VGR2776 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2776 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2776 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0623] VGR2776 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM260 precursor RNA, VGAM261 precursor RNA, VGAM262 precursor RNA, VGAM263 precursor RNA, VGAM264 precursor RNA and VGAM265 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0624] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM260 RNA, VGAM261 RNA, VGAM262 RNA, VGAM263 RNA, VGAM264 RNA and VGAM265 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0625] VGAM260 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM260 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM260 host target RNA into VGAM260 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0626] VGAM261 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM261 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM261 host target RNA into VGAM261 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0627] VGAM262 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM262 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM262 host target RNA into VGAM262 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0628] VGAM263 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM263 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM263 host target RNA into VGAM263 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0629] VGAM264 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM264 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM264 host target RNA into VGAM264 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0630] VGAM265 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM265 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM265 host target RNA into VGAM265 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0631] It is appreciated that a function of VGR2776 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2776 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2776 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2776 gene: VGAM260 host target protein, VGAM261 host target protein, VGAM262 host target protein, VGAM263 host target protein, VGAM264 host target protein and VGAM265 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM260, VGAM261, VGAM262, VGAM263, VGAM264 and VGAM265. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2777(VGR2777) viral gene, which encodes an `operon-like` cluster of novel viral micro

RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0632] VGR2777 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2777 gene was detected is described hereinabove with reference to Figs. 1-9.

[0633] VGR2777 gene encodes VGR2777 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0634] VGR2777 precursor RNA folds spatially, forming VGR2777 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2777 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2777 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0635] VGR2777 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM266 precursor RNA, VGAM267 precursor RNA, VGAM268 precursor RNA, VGAM269 precursor RNA, VGAM270 precursor RNA, VGAM271 precursor RNA, VGAM272 precursor RNA and VGAM273 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0636] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM266 RNA, VGAM267 RNA, VGAM268 RNA, VGAM269 RNA, VGAM270 RNA, VGAM271 RNA, VGAM272 RNA and VGAM273 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0637] VGAM266 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM266 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM266 host target RNA into VGAM266 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0638] VGAM267 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM267 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM267 host target RNA into VGAM267 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0639] VGAM268 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM268 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM268 host target RNA into VGAM268 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0640] VGAM269 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM269 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM269 host target RNA into VGAM269 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0641] VGAM270 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM270 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM270 host target RNA into VGAM270 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0642] VGAM271 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM271 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM271 host target RNA into VGAM271 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0643] VGAM272 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM272 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM272 host target RNA into VGAM272 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0644] VGAM273 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM273 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM273 host target RNA into VGAM273 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0645] It is appreciated that a function of VGR2777 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2777 gene include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2777 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2777 gene: VGAM266 host target protein, VGAM267 host target protein, VGAM268 host target protein, VGAM269 host target protein, VGAM270 host target protein, VGAM271 host target protein, VGAM272 host target protein and VGAM273 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM266, VGAM267, VGAM268, VGAM269, VGAM270, VGAM271, VGAM272 and VGAM273. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2778(VGR2778) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0646] VGR2778 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2778 gene was detected is described hereinabove with reference to Figs. 1-9.

[0647] VGR2778 gene encodes VGR2778 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0648] VGR2778 precursor RNA folds spatially, forming VGR2778 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2778 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2778 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0649] VGR2778 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM274 precursor RNA, VGAM275 precursor RNA, VGAM276 precursor RNA, VGAM277 precursor RNA, VGAM278 precursor RNA, VGAM279 precursor RNA, VGAM280 precursor RNA and VGAM281 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0650] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM274 RNA, VGAM275 RNA, VGAM276 RNA, VGAM277 RNA, VGAM278 RNA, VGAM279 RNA, VGAM280 RNA and VGAM281 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0651] VGAM274 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM274 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM274 host target RNA into VGAM274 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0652] VGAM275 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM275 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM275 host target RNA into VGAM275 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0653] VGAM276 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM276 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM276 host target RNA into VGAM276 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0654] VGAM277 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM277 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM277 host target RNA into VGAM277 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0655] VGAM278 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM278 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM278 host target RNA into VGAM278 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0656] VGAM279 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM279 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM279 host target RNA into VGAM279 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0657] VGAM280 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM280 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM280 host target RNA into VGAM280 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0658] VGAM281 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM281 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM281 host target RNA into VGAM281 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0659] It is appreciated that a function of VGR2778 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2778 gene include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2778 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2778 gene: VGAM274 host target protein, VGAM275 host target protein, VGAM276 host target protein, VGAM277 host target protein, VGAM278 host target protein, VGAM279 host target protein, VGAM280 host target protein and VGAM281 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM274, VGAM275, VGAM276, VGAM277, VGAM278, VGAM279, VGAM280 and VGAM281. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2779(VGR2779) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0660] VGR2779 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2779 gene was detected is described hereinabove with reference to Figs. 1-9.

[0661] VGR2779 gene encodes VGR2779 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0662] VGR2779 precursor RNA folds spatially, forming VGR2779 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2779 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2779 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0663] VGR2779 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM282 precursor RNA, VGAM283 precursor RNA, VGAM284 precursor RNA, VGAM285 precursor RNA, VGAM286 precursor RNA, VGAM287 precursor RNA, VGAM288 precursor RNA and VGAM289 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0664] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM282 RNA, VGAM283 RNA, VGAM284 RNA, VGAM285 RNA, VGAM286 RNA, VGAM287 RNA, VGAM288 RNA and VGAM289 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0665] VGAM282 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM282 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM282 host target RNA into VGAM282 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0666] VGAM283 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM283 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM283 host target RNA into VGAM283 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0667] VGAM284 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM284 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM284 host target RNA into VGAM284 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0668] VGAM285 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM285 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM285 host target RNA into VGAM285 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0669] VGAM286 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM286 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM286 host target RNA into VGAM286 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0670] VGAM287 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM287 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM287 host target RNA into VGAM287 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0671] VGAM288 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM288 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM288 host target RNA into VGAM288 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0672] VGAM289 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM289 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM289 host target RNA into VGAM289 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0673] It is appreciated that a function of VGR2779 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2779 gene include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2779 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2779 gene: VGAM282 host target protein, VGAM283 host target protein, VGAM284 host target protein, VGAM285 host target protein, VGAM286 host target protein, VGAM287 host target protein, VGAM288 host target protein and VGAM289 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM282, VGAM283, VGAM284, VGAM285, VGAM286, VGAM287, VGAM288 and VGAM289. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2780(VGR2780) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0674] VGR2780 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2780 gene was detected is described hereinabove with reference to Figs. 1-9.

[0675] VGR2780 gene encodes VGR2780 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0676] VGR2780 precursor RNA folds spatially, forming VGR2780 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2780 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2780 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0677] VGR2780 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM290 precursor RNA, VGAM291 precursor RNA, VGAM292 precursor RNA, VGAM293 precursor RNA, VGAM294 precursor RNA, VGAM295 precursor RNA, VGAM296 precursor RNA and VGAM297 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0678] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM290 RNA, VGAM291 RNA, VGAM292 RNA, VGAM293 RNA, VGAM294 RNA, VGAM295 RNA, VGAM296 RNA and VGAM297 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0679] VGAM290 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM290 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM290 host target RNA into VGAM290 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0680] VGAM291 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM291 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM291 host target RNA into VGAM291 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0681] VGAM292 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM292 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM292 host target RNA into VGAM292 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0682] VGAM293 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM293 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM293 host target RNA into VGAM293 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0683] VGAM294 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM294 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM294 host target RNA into VGAM294 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0684] VGAM295 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM295 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM295 host target RNA into VGAM295 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0685] VGAM296 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM296 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM296 host target RNA into VGAM296 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0686] VGAM297 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM297 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM297 host target RNA into VGAM297 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0687] It is appreciated that a function of VGR2780 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2780 gene include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2780 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2780 gene: VGAM290 host target protein, VGAM291 host target protein, VGAM292 host target protein, VGAM293 host target protein, VGAM294 host target protein, VGAM295 host target protein, VGAM296 host target protein and VGAM297 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM290, VGAM291, VGAM292, VGAM293, VGAM294, VGAM295, VGAM296 and VGAM297. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2781(VGR2781) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0688] VGR2781 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2781 gene was detected is described hereinabove with reference to Figs. 1-9.

[0689] VGR2781 gene encodes VGR2781 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0690] VGR2781 precursor RNA folds spatially, forming VGR2781 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2781 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2781 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0691] VGR2781 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM298 precursor RNA, VGAM299 precursor RNA, VGAM300 precursor RNA, VGAM301 precursor RNA, VGAM302 precursor RNA and VGAM303 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0692] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM298 RNA, VGAM299 RNA, VGAM300 RNA, VGAM301 RNA, VGAM302 RNA and VGAM303 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0693] VGAM298 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM298 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM298 host target RNA into VGAM298 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0694] VGAM299 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM299 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM299 host target RNA into VGAM299 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0695] VGAM300 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM300 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM300 host target RNA into VGAM300 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0696] VGAM301 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM301 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM301 host target RNA into VGAM301 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0697] VGAM302 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM302 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM302 host target RNA into VGAM302 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0698] VGAM303 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM303 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM303 host target RNA into VGAM303 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0699] It is appreciated that a function of VGR2781 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2781 gene include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2781 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2781 gene: VGAM298 host target protein, VGAM299 host target protein, VGAM300 host target protein, VGAM301 host target protein, VGAM302 host target protein and VGAM303 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM298, VGAM299, VGAM300, VGAM301, VGAM302 and VGAM303. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2782(VGR2782) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0700] VGR2782 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2782 gene was detected is described hereinabove with reference to Figs. 1-9.

[0701] VGR2782 gene encodes VGR2782 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0702] VGR2782 precursor RNA folds spatially, forming VGR2782 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2782 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2782 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0703] VGR2782 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM304 precursor RNA, VGAM305 precursor RNA and VGAM306 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0704] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM304 RNA, VGAM305 RNA and VGAM306 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0705] VGAM304 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM304 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM304 host target RNA into VGAM304 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0706] VGAM305 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM305 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM305 host target RNA into VGAM305 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0707] VGAM306 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM306 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM306 host target RNA into VGAM306 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0708] It is appreciated that a function of VGR2782 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2782 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2782 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2782 gene: VGAM304 host target protein, VGAM305 host target protein and VGAM306 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM304, VGAM305 and VGAM306. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2783(VGR2783) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0709] VGR2783 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2783 gene was detected is described hereinabove with reference to Figs. 1-9.

[0710] VGR2783 gene encodes VGR2783 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0711] VGR2783 precursor RNA folds spatially, forming VGR2783 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2783 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2783 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0712] VGR2783 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM310 precursor RNA, VGAM311 precursor RNA and VGAM312 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0713] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM310 RNA, VGAM311 RNA and VGAM312 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0714] VGAM310 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM310 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM310 host target RNA into

VGAM310 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0715] VGAM311 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM311 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM311 host target RNA into VGAM311 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0716] VGAM312 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM312 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM312 host target RNA into VGAM312 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0717] It is appreciated that a function of VGR2783 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2783 gene include diagnosis, prevention and treatment of viral infection by Pothos Latent Virus. Specific functions, and accordingly utilities, of VGR2783 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2783 gene: VGAM310 host target protein, VGAM311 host target protein and VGAM312 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM310, VGAM311 and VGAM312. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2784(VGR2784) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0718] VGR2784 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2784 gene was detected is described hereinabove with reference to Figs. 1-9.

[0719] VGR2784 gene encodes VGR2784 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0720] VGR2784 precursor RNA folds spatially, forming VGR2784 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2784 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2784 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0721] VGR2784 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM315 precursor RNA, VGAM316 precursor RNA, VGAM317 precursor RNA and VGAM318 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0722] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM315 RNA, VGAM316 RNA, VGAM317 RNA and VGAM318 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0723] VGAM315 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM315 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM315 host target RNA into VGAM315 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0724] VGAM316 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM316 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM316 host target RNA into VGAM316 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0725] VGAM317 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM317 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM317 host target RNA into VGAM317 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0726] VGAM318 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM318 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM318 host target RNA into VGAM318 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0727] It is appreciated that a function of VGR2784 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2784 gene include diagnosis, prevention and treatment of viral infection by

Cryphonectria Hypovirus 3. Specific functions, and accordingly utilities, of VGR2784 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2784 gene: VGAM315 host target protein, VGAM316 host target protein, VGAM317 host target protein and VGAM318 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM315, VGAM316, VGAM317 and VGAM318. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2785(VGR2785) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0728] VGR2785 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2785 gene was detected is described hereinabove with reference to Figs.

1-9.

[0729] VGR2785 gene encodes VGR2785 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0730] VGR2785 precursor RNA folds spatially, forming VGR2785 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2785 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2785 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0731] VGR2785 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM319 precursor RNA and VGAM320 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0732] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM319 RNA and VGAM320 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0733] VGAM319 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM319 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM319 host target RNA into VGAM319 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0734] VGAM320 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM320 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM320 host target RNA into VGAM320 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0735] It is appreciated that a function of VGR2785 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2785 gene include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGR2785 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2785 gene: VGAM319 host target protein and VGAM320 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM319 and VGAM320. Fig. 9 further provides a conceptual description of novel bioinformati-

cally detected regulatory viral gene, referred to here as Viral Genomic Record 2786(VGR2786) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0736] VGR2786 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2786 gene was detected is described hereinabove with reference to Figs. 1-9.

[0737] VGR2786 gene encodes VGR2786 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0738] VGR2786 precursor RNA folds spatially, forming VGR2786 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2786 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2786 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[0739] VGR2786 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM324 precursor RNA, VGAM325 precursor RNA and VGAM326 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0740] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM324 RNA, VGAM325 RNA and VGAM326 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0741] VGAM324 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM324 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM324 host target RNA into VGAM324 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0742] VGAM325 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM325 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM325 host target RNA into VGAM325 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0743] VGAM326 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM326 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM326 host target RNA into VGAM326 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0744] It is appreciated that a function of VGR2786 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2786 gene include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGR2786 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2786 gene: VGAM324 host target protein, VGAM325 host target protein and VGAM326 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to

VGAM324, VGAM325 and VGAM326. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2787 (VGR2787) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0745] VGR2787 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2787 gene was detected is described hereinabove with reference to Figs. 1-9.

[0746] VGR2787 gene encodes VGR2787 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0747] VGR2787 precursor RNA folds spatially, forming VGR2787 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2787 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2787 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0748] VGR2787 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM333 precursor RNA and VGAM334 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0749] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM333 RNA and VGAM334 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0750] VGAM333 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM333 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM333 host target RNA into VGAM333 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0751] VGAM334 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM334 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM334 host target RNA into VGAM334 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0752] It is appreciated that a function of VGR2787 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2787 gene include

diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2787 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2787 gene: VGAM333 host target protein and VGAM334 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM333 and VGAM334. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2788(VGR2788) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0753] VGR2788 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2788 gene was detected is described hereinabove with reference to Figs. 1-9.

- [0754] VGR2788 gene encodes VGR2788 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [0755] VGR2788 precursor RNA folds spatially, forming VGR2788 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2788 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2788 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [0756] VGR2788 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM335 precursor RNA, VGAM336 precursor RNA, VGAM337 precursor RNA, VGAM338 precursor RNA and VGAM339 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0757] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM335 RNA, VGAM336 RNA, VGAM337 RNA, VGAM338 RNA and VGAM339 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0758] VGAM335 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM335 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM335 host target RNA into VGAM335 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0759] VGAM336 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM336 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM336 host target RNA into VGAM336 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0760] VGAM337 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM337 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM337 host target RNA into VGAM337 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0761] VGAM338 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM338 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM338 host target RNA into VGAM338 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0762] VGAM339 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM339 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM339 host target RNA into VGAM339 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0763] It is appreciated that a function of VGR2788 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2788 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2788 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2788 gene: VGAM335 host target protein, VGAM336 host target protein, VGAM337 host target protein, VGAM338 host target protein and VGAM339 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM335, VGAM336, VGAM337, VGAM338 and VGAM339. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2789(VGR2789) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0764] VGR2789 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2789 gene was detected is described hereinabove with reference to Figs. 1-9.

[0765] VGR2789 gene encodes VGR2789 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0766] VGR2789 precursor RNA folds spatially, forming VGR2789 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2789 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2789 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0767] VGR2789 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM340 precursor RNA, VGAM341 precursor RNA, VGAM342 precursor RNA, VGAM343 precur-

sor RNA and VGAM344 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0768] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM340 RNA, VGAM341 RNA, VGAM342 RNA, VGAM343 RNA and VGAM344 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0769] VGAM340 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM340 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM340 host target RNA into VGAM340 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0770] VGAM341 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM341 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM341 host target RNA into VGAM341 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0771] VGAM342 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM342 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM342 host target RNA into VGAM342 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0772] VGAM343 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM343 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM343 host target RNA into VGAM343 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0773] VGAM344 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM344 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM344 host target RNA into

VGAM344 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0774] It is appreciated that a function of VGR2789 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2789 gene include diagnosis, prevention and treatment of viral infection by Tobacco Mosaic Virus. Specific functions, and accordingly utilities, of VGR2789 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2789 gene: VGAM340 host target protein, VGAM341 host target protein, VGAM342 host target protein, VGAM343 host target protein and VGAM344 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM340, VGAM341, VGAM342, VGAM343 and VGAM344. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2790(VGR2790)

viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0775] VGR2790 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2790 gene was detected is described hereinabove with reference to Figs. 1-9.

[0776] VGR2790 gene encodes VGR2790 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0777] VGR2790 precursor RNA folds spatially, forming VGR2790 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2790 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2790 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[0778] VGR2790 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM346 precursor RNA and VGAM347 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0779] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM346 RNA and VGAM347 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0780] VGAM346 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM346 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM346 host target RNA into VGAM346 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0781] VGAM347 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM347 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM347 host target RNA into VGAM347 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0782] It is appreciated that a function of VGR2790 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2790 gene include diagnosis, prevention and treatment of viral infection by Black Beetle Virus. Specific functions, and accordingly utilities, of VGR2790 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2790 gene: VGAM346 host target protein and VGAM347 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM346 and VGAM347. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2791(VGR2791) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0783] VGR2791 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2791 gene was detected is described hereinabove with reference to Figs. 1-9.

[0784] VGR2791 gene encodes VGR2791 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0785] VGR2791 precursor RNA folds spatially, forming VGR2791 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2791 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2791 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0786] VGR2791 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM348 precursor RNA and VGAM349 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0787] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM348 RNA and VGAM349 RNA, herein schematically represented

by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0788] VGAM348 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM348 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM348 host target RNA into VGAM348 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0789] VGAM349 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM349 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM349 host target RNA into

VGAM349 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0790] It is appreciated that a function of VGR2791 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2791 gene include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGR2791 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2791 gene: VGAM348 host target protein and VGAM349 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM348 and VGAM349. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2792(VGR2792) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0791] VGR2792 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2792 gene was detected is described hereinabove with reference to Figs. 1-9.

[0792] VGR2792 gene encodes VGR2792 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0793] VGR2792 precursor RNA folds spatially, forming VGR2792 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2792 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2792 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0794] VGR2792 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM

precursor RNAs, VGAM350 precursor RNA, VGAM351 precursor RNA, VGAM352 precursor RNA, VGAM353 precursor RNA, VGAM354 precursor RNA, VGAM355 precursor RNA, VGAM356 precursor RNA and VGAM357 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0795] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM350 RNA, VGAM351 RNA, VGAM352 RNA, VGAM353 RNA, VGAM354 RNA, VGAM355 RNA, VGAM356 RNA and VGAM357 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0796] VGAM350 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM350 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM350 host target RNA into VGAM350 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0797] VGAM351 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM351 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM351 host target RNA into VGAM351 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0798] VGAM352 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM352 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM352 host target RNA into VGAM352 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0799] VGAM353 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM353 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM353 host target RNA into VGAM353 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0800] VGAM354 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM354 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM354 host target RNA into VGAM354 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0801] VGAM355 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM355 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM355 host target RNA into VGAM355 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0802] VGAM356 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM356 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM356 host target RNA into VGAM356 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0803] VGAM357 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM357 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM357 host target RNA into VGAM357 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0804] It is appreciated that a function of VGR2792 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2792 gene include diagnosis, prevention and treatment of viral infection by Avian Infectious Bronchitis Virus. Specific functions, and accordingly utilities, of VGR2792 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2792 gene: VGAM350 host target protein, VGAM351 host target protein, VGAM352 host target protein, VGAM353 host target protein, VGAM354 host target protein, VGAM355 host target protein, VGAM356 host target protein and VGAM357 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM350, VGAM351, VGAM352, VGAM353, VGAM354, VGAM355, VGAM356 and VGAM357. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2793(VGR2793) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[0805] VGR2793 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2793 gene was detected is described hereinabove with reference to Figs. 1-9.

[0806] VGR2793 gene encodes VGR2793 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0807] VGR2793 precursor RNA folds spatially, forming VGR2793 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2793 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2793 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0808] VGR2793 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM

precursor RNAs, VGAM358 precursor RNA, VGAM359 precursor RNA, VGAM360 precursor RNA, VGAM361 precursor RNA, VGAM362 precursor RNA, VGAM363 precursor RNA and VGAM364 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0809] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM358 RNA, VGAM359 RNA, VGAM360 RNA, VGAM361 RNA, VGAM362 RNA, VGAM363 RNA and VGAM364 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0810] VGAM358 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM358 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM358 host target RNA into VGAM358 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0811] VGAM359 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM359 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM359 host target RNA into VGAM359 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0812] VGAM360 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM360 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM360 host target RNA into VGAM360 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0813] VGAM361 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM361 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM361 host target RNA into VGAM361 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0814] VGAM362 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM362 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM362 host target RNA into VGAM362 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0815] VGAM363 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM363 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM363 host target RNA into VGAM363 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0816] VGAM364 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM364 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM364 host target RNA into VGAM364 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0817] It is appreciated that a function of VGR2793 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2793 gene include diagnosis, prevention and treatment of viral infection by Avian Infectious Bronchitis Virus. Specific functions, and accordingly utilities, of VGR2793 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2793 gene: VGAM358 host target protein, VGAM359 host target protein, VGAM360 host target protein, VGAM361 host target protein, VGAM362 host target protein, VGAM363 host target protein and VGAM364 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM358, VGAM359, VGAM360, VGAM361, VGAM362, VGAM363 and VGAM364. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2794(VGR2794) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0818] VGR2794 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2794 gene was detected is described hereinabove with reference to Figs. 1-9.

[0819] VGR2794 gene encodes VGR2794 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0820] VGR2794 precursor RNA folds spatially, forming VGR2794 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2794 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2794 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0821] VGR2794 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM365 precursor RNA, VGAM366 precursor RNA, VGAM367 precursor RNA and VGAM368 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0822] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM365 RNA, VGAM366 RNA, VGAM367 RNA and VGAM368 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to

VGAM RNA of Fig. 1.

[0823] VGAM365 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM365 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM365 host target RNA into VGAM365 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0824] VGAM366 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM366 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM366 host target RNA into VGAM366 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0825] VGAM367 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM367 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM367 host target RNA into VGAM367 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0826] VGAM368 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM368 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM368 host target RNA into

VGAM368 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0827] It is appreciated that a function of VGR2794 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2794 gene include diagnosis, prevention and treatment of viral infection by Avian Infectious Bronchitis Virus. Specific functions, and accordingly utilities, of VGR2794 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2794 gene: VGAM365 host target protein, VGAM366 host target protein, VGAM367 host target protein and VGAM368 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM365, VGAM366, VGAM367 and VGAM368. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2795(VGR2795) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0828] VGR2795 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2795 gene was detected is described hereinabove with reference to Figs. 1-9.

[0829] VGR2795 gene encodes VGR2795 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0830] VGR2795 precursor RNA folds spatially, forming VGR2795 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2795 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2795 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0831] VGR2795 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM369 precursor RNA, VGAM370 precursor RNA, VGAM371 precursor RNA, VGAM372 precursor RNA, VGAM373 precursor RNA, VGAM374 precursor RNA and VGAM375 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0832] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM369 RNA, VGAM370 RNA, VGAM371 RNA, VGAM372 RNA, VGAM373 RNA, VGAM374 RNA and VGAM375 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0833] VGAM369 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM369 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM369 host target RNA into VGAM369 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0834] VGAM370 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM370 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM370 host target RNA into VGAM370 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0835] VGAM371 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM371 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM371 host target RNA into VGAM371 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0836] VGAM372 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM372 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM372 host target RNA into VGAM372 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0837] VGAM373 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM373 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM373 host target RNA into VGAM373 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0838] VGAM374 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM374 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM374 host target RNA into VGAM374 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0839] VGAM375 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM375 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM375 host target RNA into VGAM375 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0840] It is appreciated that a function of VGR2795 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2795 gene include diagnosis, prevention and treatment of viral infection by Avian Infectious Bronchitis Virus. Specific functions, and accordingly utilities, of VGR2795 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2795 gene: VGAM369 host target protein, VGAM370 host target protein, VGAM371 host target protein, VGAM372 host target protein, VGAM373 host target protein, VGAM374 host target

protein and VGAM375 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM369, VGAM370, VGAM371, VGAM372, VGAM373, VGAM374 and VGAM375. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2796(VGR2796) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0841] VGR2796 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2796 gene was detected is described hereinabove with reference to Figs. 1-9.

[0842] VGR2796 gene encodes VGR2796 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0843] VGR2796 precursor RNA folds spatially, forming VGR2796

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2796 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2796 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0844] VGR2796 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM376 precursor RNA and VGAM377 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0845] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM376 RNA and VGAM377 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[0846] VGAM376 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM376 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM376 host target RNA into VGAM376 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0847] VGAM377 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM377 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM377 host target RNA into VGAM377 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0848] It is appreciated that a function of VGR2796 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2796 gene include diagnosis, prevention and treatment of viral infection by Eggplant Mosaic Virus. Specific functions, and accordingly utilities, of VGR2796 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2796 gene: VGAM376 host target protein and VGAM377 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM376 and VGAM377. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2797(VGR2797) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of

which at least one host target gene is known in the art.

[0849] VGR2797 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2797 gene was detected is described hereinabove with reference to Figs. 1-9.

[0850] VGR2797 gene encodes VGR2797 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0851] VGR2797 precursor RNA folds spatially, forming VGR2797 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2797 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2797 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0852] VGR2797 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM378 precursor RNA, VGAM379 pre-

cursor RNA, VGAM380 precursor RNA and VGAM381 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0853] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM378 RNA, VGAM379 RNA, VGAM380 RNA and VGAM381 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0854] VGAM378 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM378 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM378 host target RNA into VGAM378 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0855] VGAM379 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM379 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM379 host target RNA into VGAM379 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0856] VGAM380 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM380 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM380 host target RNA into

VGAM380 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0857] VGAM381 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM381 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM381 host target RNA into VGAM381 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0858] It is appreciated that a function of VGR2797 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2797 gene include diagnosis, prevention and treatment of viral infection by Feline Immunodeficiency Virus. Specific functions, and accordingly utilities, of VGR2797 gene correlate with, and may be deduced from, the identity of the host target

genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2797 gene: VGAM378 host target protein, VGAM379 host target protein, VGAM380 host target protein and VGAM381 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM378, VGAM379, VGAM380 and VGAM381. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2798(VGR2798) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0859] VGR2798 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2798 gene was detected is described hereinabove with reference to Figs. 1-9.

[0860] VGR2798 gene encodes VGR2798 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[0861] VGR2798 precursor RNA folds spatially, forming VGR2798 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2798 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2798 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0862] VGR2798 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM382 precursor RNA, VGAM383 precursor RNA, VGAM384 precursor RNA, VGAM385 precursor RNA and VGAM386 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0863] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM382 RNA, VGAM383 RNA, VGAM384 RNA, VGAM385 RNA and VGAM386 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0864] VGAM382 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM382 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM382 host target RNA into VGAM382 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0865] VGAM383 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM383 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM383 host target RNA into VGAM383 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0866] VGAM384 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM384 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM384 host target RNA into VGAM384 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0867] VGAM385 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM385 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM385 host target RNA into VGAM385 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0868] VGAM386 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM386 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM386 host target RNA into VGAM386 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0869] It is appreciated that a function of VGR2798 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2798 gene include

diagnosis, prevention and treatment of viral infection by Hepatitis A Virus. Specific functions, and accordingly utilities, of VGR2798 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2798 gene: VGAM382 host target protein, VGAM383 host target protein, VGAM384 host target protein, VGAM385 host target protein and VGAM386 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM382, VGAM383, VGAM384, VGAM385 and VGAM386. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2799(VGR2799) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0870] VGR2799 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2799 gene was detected is described hereinabove with reference to Figs. 1–9.

[0871] VGR2799 gene encodes VGR2799 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0872] VGR2799 precursor RNA folds spatially, forming VGR2799 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2799 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2799 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[0873] VGR2799 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM387 precursor RNA, VGAM388 precursor RNA, VGAM389 precursor RNA, VGAM390 precursor RNA and VGAM391 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through

VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0874] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM387 RNA, VGAM388 RNA, VGAM389 RNA, VGAM390 RNA and VGAM391 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0875] VGAM387 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM387 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM387 host target RNA into VGAM387 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0876] VGAM388 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM388 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM388 host target RNA into VGAM388 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0877] VGAM389 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM389 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM389 host target RNA into VGAM389 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0878] VGAM390 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM390 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM390 host target RNA into VGAM390 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0879] VGAM391 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM391 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM391 host target RNA into VGAM391 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0880] It is appreciated that a function of VGR2799 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2799 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2799 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2799 gene: VGAM387 host target protein, VGAM388 host target protein, VGAM389 host target protein, VGAM390 host target protein and VGAM391 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM387, VGAM388, VGAM389, VGAM390 and VGAM391. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2800(VGR2800) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn

modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0881] VGR2800 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2800 gene was detected is described hereinabove with reference to Figs. 1-9.

[0882] VGR2800 gene encodes VGR2800 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0883] VGR2800 precursor RNA folds spatially, forming VGR2800 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2800 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2800 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0884] VGR2800 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM393 precursor RNA, VGAM394 precursor RNA, VGAM395 precursor RNA, VGAM396 precursor RNA, VGAM397 precursor RNA, VGAM398 precursor RNA, VGAM399 precursor RNA and VGAM400 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0885] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM393 RNA, VGAM394 RNA, VGAM395 RNA, VGAM396 RNA, VGAM397 RNA, VGAM398 RNA, VGAM399 RNA and VGAM400 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0886] VGAM393 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM393 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM393 host target RNA into VGAM393 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0887] VGAM394 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM394 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM394 host target RNA into VGAM394 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0888] VGAM395 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM395 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM395 host target RNA into VGAM395 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0889] VGAM396 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM396 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM396 host target RNA into VGAM396 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0890] VGAM397 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM397 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM397 host target RNA into VGAM397 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0891] VGAM398 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM398 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM398 host target RNA into VGAM398 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0892] VGAM399 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM399 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM399 host target RNA into VGAM399 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0893] VGAM400 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM400 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM400 host target RNA into VGAM400 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0894] It is appreciated that a function of VGR2800 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2800 gene include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGR2800 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2800 gene: VGAM393 host target protein, VGAM394 host target protein, VGAM395 host target protein, VGAM396 host target protein, VGAM397 host target protein, VGAM398 host target protein, VGAM399 host target protein and VGAM400 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM393, VGAM394, VGAM395, VGAM396, VGAM397, VGAM398, VGAM399 and VGAM400. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2801(VGR2801) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0895] VGR2801 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2801 gene was detected is described hereinabove with reference to Figs. 1-9.

[0896] VGR2801 gene encodes VGR2801 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0897] VGR2801 precursor RNA folds spatially, forming VGR2801 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2801 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2801 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0898] VGR2801 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM401 precursor RNA, VGAM402 precursor RNA, VGAM403 precursor RNA, VGAM404 precursor RNA, VGAM405 precursor RNA and VGAM406 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0899] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM401 RNA, VGAM402 RNA, VGAM403 RNA, VGAM404 RNA, VGAM405 RNA and VGAM406 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0900] VGAM401 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM401 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM401 host target RNA into VGAM401 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0901] VGAM402 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM402 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM402 host target RNA into VGAM402 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0902] VGAM403 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM403 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM403 host target RNA into VGAM403 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0903] VGAM404 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM404 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM404 host target RNA into VGAM404 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0904] VGAM405 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM405 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM405 host target RNA into VGAM405 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0905] VGAM406 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM406 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM406 host target RNA into VGAM406 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0906] It is appreciated that a function of VGR2801 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2801 gene include

diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGR2801 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2801 gene: VGAM401 host target protein, VGAM402 host target protein, VGAM403 host target protein, VGAM404 host target protein, VGAM405 host target protein and VGAM406 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM401, VGAM402, VGAM403, VGAM404, VGAM405 and VGAM406. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2802(VGR2802) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0907] VGR2802 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2802 gene was detected is described hereinabove with reference to Figs. 1-9.

[0908] VGR2802 gene encodes VGR2802 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0909] VGR2802 precursor RNA folds spatially, forming VGR2802 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2802 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2802 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0910] VGR2802 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM407 precursor RNA, VGAM408 precursor RNA and VGAM409 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0911] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM407 RNA, VGAM408 RNA and VGAM409 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0912] VGAM407 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM407 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM407 host target RNA into VGAM407 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0913] VGAM408 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM408 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM408 host target RNA into VGAM408 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0914] VGAM409 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM409 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM409 host target RNA into VGAM409 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0915] It is appreciated that a function of VGR2802 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2802 gene include diagnosis, prevention and treatment of viral infection by Melon Necrotic Spot Virus. Specific functions, and accordingly utilities, of VGR2802 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2802 gene: VGAM407 host target protein, VGAM408 host target protein and VGAM409 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM407, VGAM408 and VGAM409. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2803(VGR2803) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of

which at least one host target gene is known in the art.

[0916] VGR2803 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2803 gene was detected is described hereinabove with reference to Figs. 1-9.

[0917] VGR2803 gene encodes VGR2803 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0918] VGR2803 precursor RNA folds spatially, forming VGR2803 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2803 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2803 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0919] VGR2803 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM410 precursor RNA, VGAM411 pre-

cursor RNA and VGAM412 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0920] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM410 RNA, VGAM411 RNA and VGAM412 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0921] VGAM410 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM410 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM410 host target RNA into VGAM410 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0922] VGAM411 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM411 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM411 host target RNA into VGAM411 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0923] VGAM412 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM412 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM412 host target RNA into

VGAM412 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0924] It is appreciated that a function of VGR2803 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2803 gene include diagnosis, prevention and treatment of viral infection by O'nyong-nyong Virus. Specific functions, and accordingly utilities, of VGR2803 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2803 gene: VGAM410 host target protein, VGAM411 host target protein and VGAM412 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM410, VGAM411 and VGAM412. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2804(VGR2804) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0925] VGR2804 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2804 gene was detected is described hereinabove with reference to Figs. 1-9.

[0926] VGR2804 gene encodes VGR2804 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0927] VGR2804 precursor RNA folds spatially, forming VGR2804 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2804 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2804 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0928] VGR2804 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM413 precursor RNA, VGAM414 precursor RNA, VGAM415 precursor RNA, VGAM416 precursor RNA, VGAM417 precursor RNA, VGAM418 precursor RNA and VGAM419 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0929] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM413 RNA, VGAM414 RNA, VGAM415 RNA, VGAM416 RNA, VGAM417 RNA, VGAM418 RNA and VGAM419 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0930] VGAM413 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM413 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM413 host target RNA into VGAM413 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0931] VGAM414 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM414 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM414 host target RNA into VGAM414 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0932] VGAM415 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM415 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM415 host target RNA into VGAM415 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0933] VGAM416 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM416 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM416 host target RNA into VGAM416 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0934] VGAM417 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM417 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM417 host target RNA into VGAM417 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0935] VGAM418 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM418 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM418 host target RNA into VGAM418 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0936] VGAM419 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM419 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM419 host target RNA into VGAM419 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0937] It is appreciated that a function of VGR2804 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2804 gene include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGR2804 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2804 gene: VGAM413 host target protein, VGAM414 host target protein, VGAM415 host target protein, VGAM416 host target protein, VGAM417 host target protein, VGAM418 host target protein and VGAM419 host target protein, herein schemati-

cally represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM413, VGAM414, VGAM415, VGAM416, VGAM417, VGAM418 and VGAM419. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2805 (VGR2805) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0938] VGR2805 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2805 gene was detected is described hereinabove with reference to Figs. 1-9.

[0939] VGR2805 gene encodes VGR2805 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0940] VGR2805 precursor RNA folds spatially, forming VGR2805 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2805 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2805 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0941] VGR2805 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM420 precursor RNA and VGAM421 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0942] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM420 RNA and VGAM421 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0943] VGAM420 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM420 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM420 host target RNA into VGAM420 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0944] VGAM421 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM421 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM421 host target RNA into VGAM421 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0945] It is appreciated that a function of VGR2805 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2805 gene include diagnosis, prevention and treatment of viral infection by Human Papillomavirus Type 39. Specific functions, and accordingly utilities, of VGR2805 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2805 gene: VGAM420 host target protein and VGAM421 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM420 and VGAM421. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2806(VGR2806) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0946] VGR2806 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2806 gene was detected is described hereinabove with reference to Figs. 1–9.

[0947] VGR2806 gene encodes VGR2806 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0948] VGR2806 precursor RNA folds spatially, forming VGR2806 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2806 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2806 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[0949] VGR2806 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM422 precursor RNA and VGAM423 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0950] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM422 RNA and VGAM423 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0951] VGAM422 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM422 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM422 host target RNA into VGAM422 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0952] VGAM423 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM423 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM423 host target RNA into VGAM423 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0953] It is appreciated that a function of VGR2806 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2806 gene include diagnosis, prevention and treatment of viral infection by Canine Parvovirus. Specific functions, and accordingly utilities, of VGR2806 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2806 gene: VGAM422 host target protein and VGAM423 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM422 and VGAM423. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2807 (VGR2807) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0954] VGR2807 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2807 gene was detected is described hereinabove with reference to Figs. 1-9.

[0955] VGR2807 gene encodes VGR2807 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0956] VGR2807 precursor RNA folds spatially, forming VGR2807 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2807 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2807 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0957] VGR2807 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM424 precursor RNA, VGAM425 precursor RNA, VGAM426 precursor RNA, VGAM427 precursor RNA and VGAM428 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0958] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM424 RNA, VGAM425 RNA, VGAM426 RNA, VGAM427 RNA and VGAM428 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0959] VGAM424 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM424 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM424 host target RNA into VGAM424 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0960] VGAM425 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM425 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM425 host target RNA into VGAM425 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0961] VGAM426 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM426 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM426 host target RNA into VGAM426 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0962] VGAM427 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM427 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM427 host target RNA into VGAM427 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0963] VGAM428 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM428 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM428 host target RNA into VGAM428 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0964] It is appreciated that a function of VGR2807 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2807 gene include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGR2807 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2807 gene: VGAM424 host target protein,

VGAM425 host target protein, VGAM426 host target protein, VGAM427 host target protein and VGAM428 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM424, VGAM425, VGAM426, VGAM427 and VGAM428. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2808(VGR2808) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0965] VGR2808 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2808 gene was detected is described hereinabove with reference to Figs. 1-9.

[0966] VGR2808 gene encodes VGR2808 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0967] VGR2808 precursor RNA folds spatially, forming VGR2808 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2808 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2808 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0968] VGR2808 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM429 precursor RNA, VGAM430 precursor RNA, VGAM431 precursor RNA, VGAM432 precursor RNA and VGAM433 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0969] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM429

RNA, VGAM430 RNA, VGAM431 RNA, VGAM432 RNA and VGAM433 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0970] VGAM429 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM429 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM429 host target RNA into VGAM429 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0971] VGAM430 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM430 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM430 host target RNA into VGAM430 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0972] VGAM431 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM431 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM431 host target RNA into VGAM431 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0973] VGAM432 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM432 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM432 host target RNA into VGAM432 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0974] VGAM433 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM433 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM433 host target RNA into VGAM433 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0975] It is appreciated that a function of VGR2808 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2808 gene include diagnosis, prevention and treatment of viral infection by

Rabbit Hemorrhagic Disease Virus. Specific functions, and accordingly utilities, of VGR2808 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2808 gene: VGAM429 host target protein, VGAM430 host target protein, VGAM431 host target protein, VGAM432 host target protein and VGAM433 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM429, VGAM430, VGAM431, VGAM432 and VGAM433. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2809(VGR2809) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0976] VGR2809 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2809 gene was

detected is described hereinabove with reference to Figs. 1-9.

[0977] VGR2809 gene encodes VGR2809 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0978] VGR2809 precursor RNA folds spatially, forming VGR2809 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2809 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2809 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0979] VGR2809 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM434 precursor RNA, VGAM435 precursor RNA and VGAM436 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0980] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM434 RNA, VGAM435 RNA and VGAM436 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0981] VGAM434 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM434 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM434 host target RNA into VGAM434 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0982] VGAM435 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM435 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM435 host target RNA into VGAM435 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0983] VGAM436 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM436 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM436 host target RNA into VGAM436 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0984] It is appreciated that a function of VGR2809 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2809 gene include diagnosis, prevention and treatment of viral infection by Sendai Virus. Specific functions, and accordingly utilities, of VGR2809 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2809 gene: VGAM434 host target protein, VGAM435 host target protein and VGAM436 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM434, VGAM435 and VGAM436. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2810(VGR2810) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[0985] VGR2810 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2810 gene was detected is described hereinabove with reference to Figs. 1-9.

[0986] VGR2810 gene encodes VGR2810 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0987] VGR2810 precursor RNA folds spatially, forming VGR2810 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2810 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2810 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0988] VGR2810 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM437 precursor RNA, VGAM438 precursor RNA and VGAM439 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0989] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM437 RNA, VGAM438 RNA and VGAM439 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0990] VGAM437 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM437 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM437 host target RNA into VGAM437 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0991] VGAM438 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM438 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM438 host target RNA into VGAM438 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[0992] VGAM439 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM439 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM439 host target RNA into VGAM439 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[0993] It is appreciated that a function of VGR2810 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2810 gene include diagnosis, prevention and treatment of viral infection by Tomato Bushy Stunt Virus. Specific functions, and accordingly utilities, of VGR2810 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2810 gene: VGAM437 host target protein, VGAM438 host target protein and VGAM439 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM437, VGAM438 and VGAM439. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2811(VGR2811) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of

which at least one host target gene is known in the art.

[0994] VGR2811 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2811 gene was detected is described hereinabove with reference to Figs. 1-9.

[0995] VGR2811 gene encodes VGR2811 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[0996] VGR2811 precursor RNA folds spatially, forming VGR2811 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2811 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2811 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[0997] VGR2811 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM441 precursor RNA and VGAM442

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[0998] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM441 RNA and VGAM442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[0999] VGAM441 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM441 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM441 host target RNA into VGAM441 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1000] VGAM442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM442 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM442 host target RNA into VGAM442 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1001] It is appreciated that a function of VGR2811 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2811 gene include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGR2811 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2811 gene: VGAM441 host target protein and VGAM442 host target protein, herein schematically

represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM441 and VGAM442. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2812(VGR2812) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1002] VGR2812 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2812 gene was detected is described hereinabove with reference to Figs. 1-9.

[1003] VGR2812 gene encodes VGR2812 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1004] VGR2812 precursor RNA folds spatially, forming VGR2812 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2812 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2812 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1005] VGR2812 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM443 precursor RNA and VGAM444 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1006] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM443 RNA and VGAM444 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1007] VGAM443 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM443 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM443 host target RNA into VGAM443 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1008] VGAM444 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM444 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM444 host target RNA into VGAM444 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1009] It is appreciated that a function of VGR2812 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2812 gene include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGR2812 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2812 gene: VGAM443 host target protein and VGAM444 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM443 and VGAM444. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2813(VGR2813) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1010] VGR2813 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2813 gene was detected is described hereinabove with reference to Figs. 1-9.

[1011] VGR2813 gene encodes VGR2813 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1012] VGR2813 precursor RNA folds spatially, forming VGR2813 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2813 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2813 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1013] VGR2813 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM445 precursor RNA and VGAM446 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1014] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM445 RNA and VGAM446 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1015] VGAM445 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM445 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM445 host target RNA into VGAM445 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1016] VGAM446 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM446 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM446 host target RNA into VGAM446 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1017] It is appreciated that a function of VGR2813 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2813 gene include diagnosis, prevention and treatment of viral infection by Human Papillomavirus Type 17. Specific functions, and accordingly utilities, of VGR2813 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2813 gene: VGAM445 host target protein and VGAM446 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-

above with reference to VGAM445 and VGAM446. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2814 (VGR2814) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1018] VGR2814 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2814 gene was detected is described hereinabove with reference to Figs. 1-9.

[1019] VGR2814 gene encodes VGR2814 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1020] VGR2814 precursor RNA folds spatially, forming VGR2814 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2814 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2814 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1021] VGR2814 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM447 precursor RNA and VGAM448 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1022] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM447 RNA and VGAM448 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1023] VGAM447 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM447 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM447 host target RNA into VGAM447 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1024] VGAM448 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM448 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM448 host target RNA into VGAM448 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1025] It is appreciated that a function of VGR2814 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2814 gene include diagnosis, prevention and treatment of viral infection by Human Papillomavirus Type 40. Specific functions, and accordingly utilities, of VGR2814 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2814 gene: VGAM447 host target protein and VGAM448 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM447 and VGAM448. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2815(VGR2815) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1026] VGR2815 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2815 gene was

detected is described hereinabove with reference to Figs. 1-9.

[1027] VGR2815 gene encodes VGR2815 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1028] VGR2815 precursor RNA folds spatially, forming VGR2815 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2815 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2815 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1029] VGR2815 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM450 precursor RNA, VGAM451 precursor RNA and VGAM452 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1030] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM450 RNA, VGAM451 RNA and VGAM452 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1031] VGAM450 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM450 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM450 host target RNA into VGAM450 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1032] VGAM451 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM451 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM451 host target RNA into VGAM451 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1033] VGAM452 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM452 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM452 host target RNA into VGAM452 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1034] It is appreciated that a function of VGR2815 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2815 gene include diagnosis, prevention and treatment of viral infection by Cardamine Chlorotic Fleck Virus. Specific functions, and accordingly utilities, of VGR2815 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2815 gene: VGAM450 host target protein, VGAM451 host target protein and VGAM452 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM450, VGAM451 and VGAM452. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2816(VGR2816) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1035] VGR2816 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2816 gene was detected is described hereinabove with reference to Figs. 1-9.

[1036] VGR2816 gene encodes VGR2816 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1037] VGR2816 precursor RNA folds spatially, forming VGR2816 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2816 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2816 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1038] VGR2816 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM453 precursor RNA, VGAM454 precursor RNA and VGAM455 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1039] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM453 RNA, VGAM454 RNA and VGAM455 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1040] VGAM453 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM453 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM453 host target RNA into VGAM453 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1041] VGAM454 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM454 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM454 host target RNA into VGAM454 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1042] VGAM455 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM455 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM455 host target RNA into VGAM455 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1043] It is appreciated that a function of VGR2816 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2816 gene include diagnosis, prevention and treatment of viral infection by Borna Disease Virus. Specific functions, and accordingly utilities, of VGR2816 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2816 gene: VGAM453 host target protein, VGAM454 host target protein and VGAM455 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM453, VGAM454 and VGAM455. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2817(VGR2817) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1044] VGR2817 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2817 gene was detected is described hereinabove with reference to Figs. 1-9.

[1045] VGR2817 gene encodes VGR2817 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1046] VGR2817 precursor RNA folds spatially, forming VGR2817 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2817 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2817 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1047] VGR2817 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM

precursor RNAs, VGAM456 precursor RNA and VGAM457 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1048] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM456 RNA and VGAM457 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1049] VGAM456 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM456 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM456 host target RNA into VGAM456 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1050] VGAM457 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM457 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM457 host target RNA into VGAM457 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1051] It is appreciated that a function of VGR2817 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2817 gene include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR2817 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2817 gene: VGAM456 host target protein

and VGAM457 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM456 and VGAM457. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2818(VGR2818) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1052] VGR2818 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2818 gene was detected is described hereinabove with reference to Figs. 1-9.

[1053] VGR2818 gene encodes VGR2818 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1054] VGR2818 precursor RNA folds spatially, forming VGR2818 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2818 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2818 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1055] VGR2818 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM458 precursor RNA and VGAM459 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1056] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM458 RNA and VGAM459 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1057] VGAM458 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM458 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM458 host target RNA into VGAM458 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1058] VGAM459 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM459 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM459 host target RNA into VGAM459 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1059] It is appreciated that a function of VGR2818 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2818 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR2818 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2818 gene: VGAM458 host target protein and VGAM459 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM458 and VGAM459. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2819(VGR2819) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1060] VGR2819 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2819 gene was detected is described hereinabove with reference to Figs. 1-9.

[1061] VGR2819 gene encodes VGR2819 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1062] VGR2819 precursor RNA folds spatially, forming VGR2819 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2819 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2819 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1063] VGR2819 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM462 precursor RNA, VGAM463 precursor RNA and VGAM464 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1064] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM462 RNA, VGAM463 RNA and VGAM464 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1065] VGAM462 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM462 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM462 host target RNA into VGAM462 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1066] VGAM463 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM463 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM463 host target RNA into VGAM463 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1067] VGAM464 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM464 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM464 host target RNA into VGAM464 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1068] It is appreciated that a function of VGR2819 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2819 gene include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR2819 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2819 gene: VGAM462 host target protein, VGAM463 host target protein and VGAM464 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM462, VGAM463 and VGAM464. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2820(VGR2820) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene

is known in the art.

[1069] VGR2820 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2820 gene was detected is described hereinabove with reference to Figs. 1-9.

[1070] VGR2820 gene encodes VGR2820 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1071] VGR2820 precursor RNA folds spatially, forming VGR2820 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2820 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2820 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1072] VGR2820 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM466 precursor RNA and VGAM467

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1073] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM466 RNA and VGAM467 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1074] VGAM466 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM466 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM466 host target RNA into VGAM466 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1075] VGAM467 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM467 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM467 host target RNA into VGAM467 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1076] It is appreciated that a function of VGR2820 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2820 gene include diagnosis, prevention and treatment of viral infection by Autographa Californica Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2820 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2820 gene: VGAM466 host target protein and VGAM467 host target

protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM466 and VGAM467. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2821 (VGR2821) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1077] VGR2821 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2821 gene was detected is described hereinabove with reference to Figs. 1-9.

[1078] VGR2821 gene encodes VGR2821 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1079] VGR2821 precursor RNA folds spatially, forming VGR2821 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2821 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2821 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1080] VGR2821 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM472 precursor RNA, VGAM473 precursor RNA, VGAM474 precursor RNA, VGAM475 precursor RNA and VGAM476 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1081] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM472 RNA, VGAM473 RNA, VGAM474 RNA, VGAM475 RNA and VGAM476 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[1082] VGAM472 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM472 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM472 host target RNA into VGAM472 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1083] VGAM473 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM473 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM473 host target RNA into VGAM473 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1084] VGAM474 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM474 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM474 host target RNA into VGAM474 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1085] VGAM475 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM475 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM475 host target RNA into

VGAM475 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1086] VGAM476 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM476 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM476 host target RNA into VGAM476 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1087] It is appreciated that a function of VGR2821 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2821 gene include diagnosis, prevention and treatment of viral infection by Tick-borne Encephalitis Virus. Specific functions, and accordingly utilities, of VGR2821 gene correlate with, and may be deduced from, the identity of the host target

genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2821 gene: VGAM472 host target protein, VGAM473 host target protein, VGAM474 host target protein, VGAM475 host target protein and VGAM476 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM472, VGAM473, VGAM474, VGAM475 and VGAM476. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2822(VGR2822) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1088] VGR2822 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2822 gene was detected is described hereinabove with reference to Figs. 1-9.

[1089] VGR2822 gene encodes VGR2822 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1090] VGR2822 precursor RNA folds spatially, forming VGR2822 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2822 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2822 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1091] VGR2822 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM477 precursor RNA, VGAM478 precursor RNA, VGAM479 precursor RNA, VGAM480 precursor RNA, VGAM481 precursor RNA, VGAM482 precursor RNA, VGAM483 precursor RNA and VGAM484 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR

RNA of Fig. 1.

[1092] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM477 RNA, VGAM478 RNA, VGAM479 RNA, VGAM480 RNA, VGAM481 RNA, VGAM482 RNA, VGAM483 RNA and VGAM484 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1093] VGAM477 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM477 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM477 host target RNA into VGAM477 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1094] VGAM478 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM478 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM478 host target RNA into VGAM478 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1095] VGAM479 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM479 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM479 host target RNA into VGAM479 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1096] VGAM480 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM480 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM480 host target RNA into VGAM480 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1097] VGAM481 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM481 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM481 host target RNA into VGAM481 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1098] VGAM482 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM482 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM482 host target RNA into VGAM482 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1099] VGAM483 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM483 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM483 host target RNA into VGAM483 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1100] VGAM484 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM484 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM484 host target RNA into VGAM484 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1101] It is appreciated that a function of VGR2822 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2822 gene include diagnosis, prevention and treatment of viral infection by Hepatitis G Virus. Specific functions, and accordingly utilities, of VGR2822 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2822 gene: VGAM477 host

target protein, VGAM478 host target protein, VGAM479 host target protein, VGAM480 host target protein, VGAM481 host target protein, VGAM482 host target protein, VGAM483 host target protein and VGAM484 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM477, VGAM478, VGAM479, VGAM480, VGAM481, VGAM482, VGAM483 and VGAM484. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2823(VGR2823) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1102] VGR2823 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2823 gene was detected is described hereinabove with reference to Figs. 1-9.

[1103] VGR2823 gene encodes VGR2823 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1104] VGR2823 precursor RNA folds spatially, forming VGR2823 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2823 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2823 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1105] VGR2823 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM485 precursor RNA, VGAM486 precursor RNA, VGAM487 precursor RNA, VGAM488 precursor RNA, VGAM489 precursor RNA, VGAM490 precursor RNA, VGAM491 precursor RNA and VGAM492 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR

RNA of Fig. 1.

[1106] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM485 RNA, VGAM486 RNA, VGAM487 RNA, VGAM488 RNA, VGAM489 RNA, VGAM490 RNA, VGAM491 RNA and VGAM492 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1107] VGAM485 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM485 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM485 host target RNA into VGAM485 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1108] VGAM486 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM486 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM486 host target RNA into VGAM486 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1109] VGAM487 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM487 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM487 host target RNA into VGAM487 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1110] VGAM488 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM488 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM488 host target RNA into VGAM488 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1111] VGAM489 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM489 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM489 host target RNA into VGAM489 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1112] VGAM490 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM490 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM490 host target RNA into VGAM490 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1113] VGAM491 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM491 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM491 host target RNA into VGAM491 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1114] VGAM492 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM492 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM492 host target RNA into VGAM492 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1115] It is appreciated that a function of VGR2823 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2823 gene include diagnosis, prevention and treatment of viral infection by Hepatitis G Virus. Specific functions, and accordingly utilities, of VGR2823 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2823 gene: VGAM485 host

target protein, VGAM486 host target protein, VGAM487 host target protein, VGAM488 host target protein, VGAM489 host target protein, VGAM490 host target protein, VGAM491 host target protein and VGAM492 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM485, VGAM486, VGAM487, VGAM488, VGAM489, VGAM490, VGAM491 and VGAM492. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2824(VGR2824) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1116] VGR2824 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2824 gene was detected is described hereinabove with reference to Figs. 1-9.

[1117] VGR2824 gene encodes VGR2824 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1118] VGR2824 precursor RNA folds spatially, forming VGR2824 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2824 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2824 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1119] VGR2824 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM493 precursor RNA, VGAM494 precursor RNA and VGAM495 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1120] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM493 RNA, VGAM494 RNA and VGAM495 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1121] VGAM493 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM493 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM493 host target RNA into VGAM493 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1122] VGAM494 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM494 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM494 host target RNA into VGAM494 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1123] VGAM495 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM495 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM495 host target RNA into VGAM495 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1124] It is appreciated that a function of VGR2824 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2824 gene include

diagnosis, prevention and treatment of viral infection by Hepatitis G Virus. Specific functions, and accordingly utilities, of VGR2824 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2824 gene: VGAM493 host target protein, VGAM494 host target protein and VGAM495 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM493, VGAM494 and VGAM495. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2825(VGR2825) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1125] VGR2825 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2825 gene was detected is described hereinabove with reference to Figs.

1-9.

- [1126] VGR2825 gene encodes VGR2825 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1127] VGR2825 precursor RNA folds spatially, forming VGR2825 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2825 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2825 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1128] VGR2825 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM496 precursor RNA and VGAM497 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1129] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM496 RNA and VGAM497 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1130] VGAM496 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM496 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM496 host target RNA into VGAM496 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1131] VGAM497 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM497 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM497 host target RNA into VGAM497 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1132] It is appreciated that a function of VGR2825 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2825 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2825 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2825 gene: VGAM496 host target protein and VGAM497 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM496 and VGAM497. Fig. 9 further provides a conceptual description of novel bioinformati-

cally detected regulatory viral gene, referred to here as Viral Genomic Record 2826(VGR2826) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1133] VGR2826 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2826 gene was detected is described hereinabove with reference to Figs. 1-9.

[1134] VGR2826 gene encodes VGR2826 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1135] VGR2826 precursor RNA folds spatially, forming VGR2826 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2826 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2826 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1136] VGR2826 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM499 precursor RNA and VGAM500 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1137] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM499 RNA and VGAM500 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1138] VGAM499 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM499 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM499 host target RNA into VGAM499 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1139] VGAM500 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM500 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM500 host target RNA into VGAM500 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1140] It is appreciated that a function of VGR2826 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2826 gene include diagnosis, prevention and treatment of viral infection by Strawberry Vein Banding Virus (SVBV). Specific functions,

and accordingly utilities, of VGR2826 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2826 gene: VGAM499 host target protein and VGAM500 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM499 and VGAM500. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2827(VGR2827) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1141] VGR2827 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2827 gene was detected is described hereinabove with reference to Figs. 1-9.

[1142] VGR2827 gene encodes VGR2827 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1143] VGR2827 precursor RNA folds spatially, forming VGR2827 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2827 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2827 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1144] VGR2827 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM501 precursor RNA and VGAM502 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1145] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM501 RNA and VGAM502 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1146] VGAM501 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM501 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM501 host target RNA into VGAM501 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1147] VGAM502 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM502 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM502 host target RNA into VGAM502 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1148] It is appreciated that a function of VGR2827 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2827 gene include diagnosis, prevention and treatment of viral infection by Carrot Mottle Mimic Virus. Specific functions, and accordingly utilities, of VGR2827 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2827 gene: VGAM501 host target protein and VGAM502 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM501 and VGAM502. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2828(VGR2828) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1149] VGR2828 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2828 gene was detected is described hereinabove with reference to Figs. 1-9.

[1150] VGR2828 gene encodes VGR2828 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1151] VGR2828 precursor RNA folds spatially, forming VGR2828 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2828 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2828 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1152] VGR2828 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM506 precursor RNA, VGAM507 precursor RNA and VGAM508 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1153] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM506 RNA, VGAM507 RNA and VGAM508 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1154] VGAM506 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM506 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM506 host target RNA into VGAM506 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1155] VGAM507 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM507 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM507 host target RNA into VGAM507 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1156] VGAM508 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM508 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM508 host target RNA into VGAM508 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1157] It is appreciated that a function of VGR2828 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2828 gene include diagnosis, prevention and treatment of viral infection by Saguaro Cactus Virus. Specific functions, and accordingly utilities, of VGR2828 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2828 gene: VGAM506 host target protein, VGAM507 host target protein and VGAM508 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM506, VGAM507 and VGAM508. Fig. 9 further provides a conceptual description of novel bioinformatically

detected regulatory viral gene, referred to here as Viral Genomic Record 2829(VGR2829) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1158] VGR2829 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2829 gene was detected is described hereinabove with reference to Figs. 1-9.

[1159] VGR2829 gene encodes VGR2829 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1160] VGR2829 precursor RNA folds spatially, forming VGR2829 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2829 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2829 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1161] VGR2829 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM509 precursor RNA and VGAM510 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1162] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM509 RNA and VGAM510 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1163] VGAM509 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM509 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM509 host target RNA into VGAM509 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1164] VGAM510 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM510 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM510 host target RNA into VGAM510 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1165] It is appreciated that a function of VGR2829 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2829 gene include diagnosis, prevention and treatment of viral infection by Papaya Ringspot Virus. Specific functions, and accordingly

utilities, of VGR2829 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2829 gene: VGAM509 host target protein and VGAM510 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM509 and VGAM510. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2830(VGR2830) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1166] VGR2830 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2830 gene was detected is described hereinabove with reference to Figs. 1-9.

[1167] VGR2830 gene encodes VGR2830 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[1168] VGR2830 precursor RNA folds spatially, forming VGR2830 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2830 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2830 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1169] VGR2830 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM511 precursor RNA, VGAM512 precursor RNA, VGAM513 precursor RNA, VGAM514 precursor RNA and VGAM515 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1170] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM511 RNA, VGAM512 RNA, VGAM513 RNA, VGAM514 RNA and VGAM515 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1171] VGAM511 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM511 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM511 host target RNA into VGAM511 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1172] VGAM512 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM512 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM512 host target RNA into VGAM512 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1173] VGAM513 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM513 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM513 host target RNA into VGAM513 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1174] VGAM514 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM514 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM514 host target RNA into VGAM514 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1175] VGAM515 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM515 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM515 host target RNA into VGAM515 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1176] It is appreciated that a function of VGR2830 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2830 gene include

diagnosis, prevention and treatment of viral infection by Cucumber Green Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGR2830 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2830 gene: VGAM511 host target protein, VGAM512 host target protein, VGAM513 host target protein, VGAM514 host target protein and VGAM515 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM511, VGAM512, VGAM513, VGAM514 and VGAM515. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2831(VGR2831) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1177] VGR2831 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2831 gene was detected is described hereinabove with reference to Figs. 1-9.

[1178] VGR2831 gene encodes VGR2831 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1179] VGR2831 precursor RNA folds spatially, forming VGR2831 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2831 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2831 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1180] VGR2831 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM516 precursor RNA and VGAM517 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1181] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM516 RNA and VGAM517 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1182] VGAM516 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM516 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM516 host target RNA into VGAM516 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1183] VGAM517 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM517 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM517 host target RNA into VGAM517 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1184] It is appreciated that a function of VGR2831 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2831 gene include diagnosis, prevention and treatment of viral infection by Galinsoga Mosaic Virus. Specific functions, and accordingly utilities, of VGR2831 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2831 gene: VGAM516 host target protein and VGAM517 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove

with reference to VGAM516 and VGAM517. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2832 (VGR2832) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1185] VGR2832 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2832 gene was detected is described hereinabove with reference to Figs. 1-9.

[1186] VGR2832 gene encodes VGR2832 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1187] VGR2832 precursor RNA folds spatially, forming VGR2832 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2832 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2832 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1188] VGR2832 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM519 precursor RNA and VGAM520 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1189] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM519 RNA and VGAM520 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1190] VGAM519 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM519 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM519 host target RNA into VGAM519 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1191] VGAM520 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM520 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM520 host target RNA into VGAM520 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1192] It is appreciated that a function of VGR2832 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2832 gene include

diagnosis, prevention and treatment of viral infection by Lymphocystis Disease Virus 1. Specific functions, and accordingly utilities, of VGR2832 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2832 gene: VGAM519 host target protein and VGAM520 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM519 and VGAM520. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2833(VGR2833) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1193] VGR2833 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2833 gene was detected is described hereinabove with reference to Figs.

1-9.

- [1194] VGR2833 gene encodes VGR2833 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1195] VGR2833 precursor RNA folds spatially, forming VGR2833 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2833 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2833 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1196] VGR2833 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM521 precursor RNA and VGAM522 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1197] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM521 RNA and VGAM522 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1198] VGAM521 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM521 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM521 host target RNA into VGAM521 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1199] VGAM522 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM522 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM522 host target RNA into VGAM522 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1200] It is appreciated that a function of VGR2833 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2833 gene include diagnosis, prevention and treatment of viral infection by Lymphocystis Disease Virus 1. Specific functions, and accordingly utilities, of VGR2833 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2833 gene: VGAM521 host target protein and VGAM522 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM521 and VGAM522. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 2834(VGR2834) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1201] VGR2834 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2834 gene was detected is described hereinabove with reference to Figs. 1-9.

[1202] VGR2834 gene encodes VGR2834 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1203] VGR2834 precursor RNA folds spatially, forming VGR2834 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2834 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2834 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1204] VGR2834 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM523 precursor RNA and VGAM524 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1205] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM523 RNA and VGAM524 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1206] VGAM523 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM523 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM523 host target RNA into VGAM523 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1207] VGAM524 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM524 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM524 host target RNA into VGAM524 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1208] It is appreciated that a function of VGR2834 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2834 gene include diagnosis, prevention and treatment of viral infection by

Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2834 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2834 gene: VGAM523 host target protein and VGAM524 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM523 and VGAM524. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2835(VGR2835) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1209] VGR2835 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2835 gene was detected is described hereinabove with reference to Figs. 1-9.

[1210] VGR2835 gene encodes VGR2835 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1211] VGR2835 precursor RNA folds spatially, forming VGR2835 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2835 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2835 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1212] VGR2835 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM525 precursor RNA and VGAM526 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1213] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM525 RNA and VGAM526 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1214] VGAM525 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM525 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM525 host target RNA into VGAM525 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1215] VGAM526 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM526 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM526 host target RNA into VGAM526 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1216] It is appreciated that a function of VGR2835 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2835 gene include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2835 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2835 gene: VGAM525 host target protein and VGAM526 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM525 and VGAM526. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2836(VGR2836) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1217] VGR2836 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2836 gene was detected is described hereinabove with reference to Figs. 1-9.

[1218] VGR2836 gene encodes VGR2836 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1219] VGR2836 precursor RNA folds spatially, forming VGR2836 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2836 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2836 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1220] VGR2836 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM536 precursor RNA and VGAM537 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1221] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM536 RNA and VGAM537 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1222] VGAM536 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM536 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM536 host target RNA into

VGAM536 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1223] VGAM537 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM537 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM537 host target RNA into VGAM537 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1224] It is appreciated that a function of VGR2836 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2836 gene include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2836 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2836 gene: VGAM536 host
target protein and VGAM537 host target protein, herein
schematically represented by VGAM1 HOST TARGET PRO-
TEIN through VGAM3 HOST TARGET PROTEIN. The func-
tion of these host target genes is elaborated hereinabove
with reference to VGAM536 and VGAM537. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 2837(VGR2837) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[1225] VGR2837 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2837 gene was
detected is described hereinabove with reference to Figs.
1-9.

[1226] VGR2837 gene encodes VGR2837 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[1227] VGR2837 precursor RNA folds spatially, forming VGR2837

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2837 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2837 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1228] VGR2837 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM539 precursor RNA, VGAM540 precursor RNA and VGAM541 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1229] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM539 RNA, VGAM540 RNA and VGAM541 RNA, herein schemati-

cally represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1230] VGAM539 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM539 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM539 host target RNA into VGAM539 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1231] VGAM540 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM540 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM540 host target RNA into VGAM540 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1232] VGAM541 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM541 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM541 host target RNA into VGAM541 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1233] It is appreciated that a function of VGR2837 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2837 gene include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGR2837 gene correlate with, and

may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2837 gene: VGAM539 host target protein, VGAM540 host target protein and VGAM541 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM539, VGAM540 and VGAM541. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2838(VGR2838) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1234] VGR2838 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2838 gene was detected is described hereinabove with reference to Figs. 1-9.

[1235] VGR2838 gene encodes VGR2838 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[1236] VGR2838 precursor RNA folds spatially, forming VGR2838 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2838 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2838 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1237] VGR2838 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM546 precursor RNA and VGAM547 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1238] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM546

RNA and VGAM547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1239] VGAM546 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM546 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM546 host target RNA into VGAM546 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1240] VGAM547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM547 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM547 host target RNA into VGAM547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1241] It is appreciated that a function of VGR2838 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2838 gene include diagnosis, prevention and treatment of viral infection by Peanut Stunt Virus. Specific functions, and accordingly utilities, of VGR2838 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2838 gene: VGAM546 host target protein and VGAM547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM546 and VGAM547. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2839(VGR2839) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1242] VGR2839 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2839 gene was detected is described hereinabove with reference to Figs. 1-9.

[1243] VGR2839 gene encodes VGR2839 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1244] VGR2839 precursor RNA folds spatially, forming VGR2839 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2839 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2839 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1245] VGR2839 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM550 precursor RNA and VGAM551 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1246] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM550 RNA and VGAM551 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1247] VGAM550 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM550 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM550 host target RNA into VGAM550 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1248] VGAM551 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM551 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM551 host target RNA into VGAM551 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1249] It is appreciated that a function of VGR2839 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2839 gene include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 2-1. Specific functions, and accordingly utilities, of VGR2839 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2839 gene: VGAM550 host target protein and VGAM551 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM550 and VGAM551. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2840(VGR2840) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1250] VGR2840 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2840 gene was detected is described hereinabove with reference to Figs. 1-9.

[1251] VGR2840 gene encodes VGR2840 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1252] VGR2840 precursor RNA folds spatially, forming VGR2840 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2840 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2840 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1253] VGR2840 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM554 precursor RNA, VGAM555 precursor RNA and VGAM556 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1254] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM554 RNA, VGAM555 RNA and VGAM556 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA,

each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1255] VGAM554 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM554 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM554 host target RNA into VGAM554 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1256] VGAM555 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM555 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM555 host target RNA into

VGAM555 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1257] VGAM556 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM556 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM556 host target RNA into VGAM556 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1258] It is appreciated that a function of VGR2840 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2840 gene include diagnosis, prevention and treatment of viral infection by Spodoptera Exigua Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2840 gene correlate with, and may be deduced from, the identity of the host

target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2840 gene: VGAM554 host target protein, VGAM555 host target protein and VGAM556 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM554, VGAM555 and VGAM556. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2841(VGR2841) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1259] VGR2841 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2841 gene was detected is described hereinabove with reference to Figs. 1-9.

[1260] VGR2841 gene encodes VGR2841 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[1261] VGR2841 precursor RNA folds spatially, forming VGR2841 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2841 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2841 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1262] VGR2841 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM562 precursor RNA, VGAM563 precursor RNA and VGAM564 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1263] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM562 RNA, VGAM563 RNA and VGAM564 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1264] VGAM562 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM562 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM562 host target RNA into VGAM562 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1265] VGAM563 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM563 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM563 host target RNA into VGAM563 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1266] VGAM564 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM564 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM564 host target RNA into VGAM564 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1267] It is appreciated that a function of VGR2841 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2841 gene include diagnosis, prevention and treatment of viral infection by

Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2841 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2841 gene: VGAM562 host target protein, VGAM563 host target protein and VGAM564 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM562, VGAM563 and VGAM564. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2842(VGR2842) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1268] VGR2842 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2842 gene was detected is described hereinabove with reference to Figs. 1-9.

- [1269] VGR2842 gene encodes VGR2842 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1270] VGR2842 precursor RNA folds spatially, forming VGR2842 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2842 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2842 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1271] VGR2842 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM565 precursor RNA and VGAM566 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.
- [1272] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM565 RNA and VGAM566 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1273] VGAM565 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM565 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM565 host target RNA into VGAM565 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1274] VGAM566 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM566 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM566 host target RNA into VGAM566 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1275] It is appreciated that a function of VGR2842 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2842 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2842 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2842 gene: VGAM565 host target protein and VGAM566 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM565 and VGAM566. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Vi-

ral Genomic Record 2843(VGR2843) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1276] VGR2843 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2843 gene was detected is described hereinabove with reference to Figs. 1-9.

[1277] VGR2843 gene encodes VGR2843 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1278] VGR2843 precursor RNA folds spatially, forming VGR2843 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2843 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2843 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

- [1279] VGR2843 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM567 precursor RNA, VGAM568 precursor RNA, VGAM569 precursor RNA and VGAM570 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.
- [1280] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM567 RNA, VGAM568 RNA, VGAM569 RNA and VGAM570 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [1281] VGAM567 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM567 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM567 host target RNA into VGAM567 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1282] VGAM568 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM568 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM568 host target RNA into VGAM568 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1283] VGAM569 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM569 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM569 host target RNA into VGAM569 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1284] VGAM570 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM570 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM570 host target RNA into VGAM570 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1285] It is appreciated that a function of VGR2843 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2843 gene include

diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2843 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2843 gene: VGAM567 host target protein, VGAM568 host target protein, VGAM569 host target protein and VGAM570 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM567, VGAM568, VGAM569 and VGAM570. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2844(VGR2844) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1286] VGR2844 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2844 gene was

detected is described hereinabove with reference to Figs. 1-9.

[1287] VGR2844 gene encodes VGR2844 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1288] VGR2844 precursor RNA folds spatially, forming VGR2844 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2844 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2844 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1289] VGR2844 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM571 precursor RNA, VGAM572 precursor RNA, VGAM573 precursor RNA and VGAM574 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin

shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1290] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM571 RNA, VGAM572 RNA, VGAM573 RNA and VGAM574 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1291] VGAM571 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM571 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM571 host target RNA into VGAM571 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1292] VGAM572 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM572 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM572 host target RNA into VGAM572 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1293] VGAM573 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM573 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM573 host target RNA into VGAM573 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1294] VGAM574 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM574 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM574 host target RNA into VGAM574 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1295] It is appreciated that a function of VGR2844 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2844 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2844 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2844 gene: VGAM571 host target protein, VGAM572 host target protein, VGAM573 host target protein and VGAM574 host target protein,

herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM571, VGAM572, VGAM573 and VGAM574. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2845(VGR2845) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1296] VGR2845 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2845 gene was detected is described hereinabove with reference to Figs. 1–9.

[1297] VGR2845 gene encodes VGR2845 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1298] VGR2845 precursor RNA folds spatially, forming VGR2845 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2845 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2845 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1299] VGR2845 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM575 precursor RNA and VGAM576 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1300] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM575 RNA and VGAM576 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1301] VGAM575 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM575 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM575 host target RNA into VGAM575 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1302] VGAM576 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM576 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM576 host target RNA into VGAM576 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1303] It is appreciated that a function of VGR2845 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2845 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2845 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2845 gene: VGAM575 host target protein and VGAM576 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM575 and VGAM576. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2846(VGR2846) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1304] VGR2846 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2846 gene was detected is described hereinabove with reference to Figs. 1-9.

[1305] VGR2846 gene encodes VGR2846 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1306] VGR2846 precursor RNA folds spatially, forming VGR2846 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2846 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2846 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1307] VGR2846 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM577 precursor RNA and VGAM578 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1308] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM577 RNA and VGAM578 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1309] VGAM577 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM577 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM577 host target RNA into VGAM577 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1310] VGAM578 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM578 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM578 host target RNA into VGAM578 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1311] It is appreciated that a function of VGR2846 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2846 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2846 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2846 gene: VGAM577 host target protein and VGAM578 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM577 and VGAM578. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2847 (VGR2847) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1312] VGR2847 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2847 gene was detected is described hereinabove with reference to Figs. 1-9.

[1313] VGR2847 gene encodes VGR2847 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1314] VGR2847 precursor RNA folds spatially, forming VGR2847 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2847 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2847 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1315] VGR2847 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM580 precursor RNA and VGAM581 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1316] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM580 RNA and VGAM581 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1317] VGAM580 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM580 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM580 host target RNA into VGAM580 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1318] VGAM581 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM581 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM581 host target RNA into VGAM581 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1319] It is appreciated that a function of VGR2847 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2847 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2847 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2847 gene: VGAM580 host target protein and VGAM581 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM580 and VGAM581. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2848(VGR2848) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1320] VGR2848 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2848 gene was detected is described hereinabove with reference to Figs.

1-9.

- [1321] VGR2848 gene encodes VGR2848 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1322] VGR2848 precursor RNA folds spatially, forming VGR2848 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2848 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2848 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1323] VGR2848 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM585 precursor RNA, VGAM586 precursor RNA and VGAM587 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[1324] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM585 RNA, VGAM586 RNA and VGAM587 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1325] VGAM585 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM585 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM585 host target RNA into VGAM585 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1326] VGAM586 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM586 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM586 host target RNA into VGAM586 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1327] VGAM587 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM587 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM587 host target RNA into VGAM587 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1328] It is appreciated that a function of VGR2848 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2848 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2848 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2848 gene: VGAM585 host target protein, VGAM586 host target protein and VGAM587 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM585, VGAM586 and VGAM587. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2849(VGR2849) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1329] VGR2849 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2849 gene was detected is described hereinabove with reference to Figs. 1–9.

[1330] VGR2849 gene encodes VGR2849 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1331] VGR2849 precursor RNA folds spatially, forming VGR2849 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2849 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2849 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1332] VGR2849 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM588 precursor RNA, VGAM589 precursor RNA and VGAM590 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1333] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM588 RNA, VGAM589 RNA and VGAM590 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1334] VGAM588 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM588 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM588 host target RNA into VGAM588 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1335] VGAM589 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM589 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM589 host target RNA into VGAM589 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1336] VGAM590 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM590 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM590 host target RNA into VGAM590 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1337] It is appreciated that a function of VGR2849 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2849 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2849 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2849 gene: VGAM588 host target protein, VGAM589 host target protein and VGAM590 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM588, VGAM589 and VGAM590. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2850(VGR2850) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1338] VGR2850 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2850 gene was detected is described hereinabove with reference to Figs. 1–9.

[1339] VGR2850 gene encodes VGR2850 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1340] VGR2850 precursor RNA folds spatially, forming VGR2850 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2850 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2850 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1341] VGR2850 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM591 precursor RNA and VGAM592 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1342] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM591 RNA and VGAM592 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1343] VGAM591 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM591 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM591 host target RNA into VGAM591 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1344] VGAM592 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM592 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM592 host target RNA into VGAM592 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1345] It is appreciated that a function of VGR2850 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2850 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2850 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2850 gene: VGAM591 host target protein and VGAM592 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM591 and VGAM592. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2851 (VGR2851) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1346] VGR2851 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2851 gene was detected is described hereinabove with reference to Figs. 1-9.

[1347] VGR2851 gene encodes VGR2851 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1348] VGR2851 precursor RNA folds spatially, forming VGR2851 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2851 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2851 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1349] VGR2851 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM594 precursor RNA, VGAM595 precursor RNA and VGAM596 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1350] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM594 RNA, VGAM595 RNA and VGAM596 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1351] VGAM594 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM594 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM594 host target RNA into VGAM594 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1352] VGAM595 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM595 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM595 host target RNA into VGAM595 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1353] VGAM596 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM596 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM596 host target RNA into VGAM596 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1354] It is appreciated that a function of VGR2851 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2851 gene include diagnosis, prevention and treatment of viral infection by Northern Cereal Mosaic Virus. Specific functions, and accordingly utilities, of VGR2851 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2851 gene: VGAM594 host target protein, VGAM595 host target protein and

VGAM596 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM594, VGAM595 and VGAM596. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2852 (VGR2852) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1355] VGR2852 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2852 gene was detected is described hereinabove with reference to Figs. 1-9.

[1356] VGR2852 gene encodes VGR2852 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1357] VGR2852 precursor RNA folds spatially, forming VGR2852 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2852 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2852 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1358] VGR2852 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM597 precursor RNA, VGAM598 precursor RNA, VGAM599 precursor RNA, VGAM600 precursor RNA, VGAM601 precursor RNA, VGAM602 precursor RNA, VGAM603 precursor RNA and VGAM604 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1359] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM597 RNA, VGAM598 RNA, VGAM599 RNA, VGAM600 RNA,

VGAM601 RNA, VGAM602 RNA, VGAM603 RNA and VGAM604 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1360] VGAM597 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM597 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM597 host target RNA into VGAM597 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1361] VGAM598 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM598 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM598 host target RNA into VGAM598 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1362] VGAM599 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM599 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM599 host target RNA into VGAM599 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1363] VGAM600 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM600 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM600 host target RNA into VGAM600 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1364] VGAM601 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM601 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM601 host target RNA into VGAM601 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1365] VGAM602 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM602 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM602 host target RNA into VGAM602 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1366] VGAM603 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM603 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM603 host target RNA into VGAM603 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1367] VGAM604 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM604 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM604 host target RNA into VGAM604 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1368] It is appreciated that a function of VGR2852 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2852 gene include diagnosis, prevention and treatment of viral infection by Transmissible Gastroenteritis Virus. Specific functions, and accordingly utilities, of VGR2852 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2852 gene: VGAM597 host target protein, VGAM598 host target protein, VGAM599 host target protein, VGAM600 host target protein, VGAM601 host target protein, VGAM602 host target protein, VGAM603 host target protein and VGAM604 host target protein, herein schematically represented by

VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM597, VGAM598, VGAM599, VGAM600, VGAM601, VGAM602, VGAM603 and VGAM604. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2853(VGR2853) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1369] VGR2853 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2853 gene was detected is described hereinabove with reference to Figs. 1-9.

[1370] VGR2853 gene encodes VGR2853 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1371] VGR2853 precursor RNA folds spatially, forming VGR2853 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2853 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2853 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1372] VGR2853 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM605 precursor RNA and VGAM606 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1373] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM605 RNA and VGAM606 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1374] VGAM605 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM605 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM605 host target RNA into VGAM605 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1375] VGAM606 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM606 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM606 host target RNA into VGAM606 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1376] It is appreciated that a function of VGR2853 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2853 gene include diagnosis, prevention and treatment of viral infection by Transmissible Gastroenteritis Virus. Specific functions, and accordingly utilities, of VGR2853 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2853 gene: VGAM605 host target protein and VGAM606 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM605 and VGAM606. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2854(VGR2854) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1377] VGR2854 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2854 gene was detected is described hereinabove with reference to Figs. 1–9.

[1378] VGR2854 gene encodes VGR2854 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1379] VGR2854 precursor RNA folds spatially, forming VGR2854 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2854 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2854 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1380] VGR2854 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM607 precursor RNA, VGAM608 precursor RNA, VGAM609 precursor RNA and VGAM610 pre–

cursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1381] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM607 RNA, VGAM608 RNA, VGAM609 RNA and VGAM610 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1382] VGAM607 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM607 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM607 host target RNA into VGAM607 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1383] VGAM608 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM608 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM608 host target RNA into VGAM608 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1384] VGAM609 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM609 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM609 host target RNA into VGAM609 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1385] VGAM610 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM610 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM610 host target RNA into VGAM610 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1386] It is appreciated that a function of VGR2854 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2854 gene include diagnosis, prevention and treatment of viral infection by Rice Grassy Stunt Virus. Specific functions, and accordingly utilities, of VGR2854 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2854 gene: VGAM607 host target protein, VGAM608 host target protein, VGAM609 host target protein and VGAM610 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM607, VGAM608, VGAM609 and VGAM610. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2855(VGR2855) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1387] VGR2855 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2855 gene was detected is described hereinabove with reference to Figs. 1-9.

[1388] VGR2855 gene encodes VGR2855 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1389] VGR2855 precursor RNA folds spatially, forming VGR2855 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2855 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2855 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1390] VGR2855 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM613 precursor RNA and VGAM614 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1391] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM613 RNA and VGAM614 RNA, herein schematically represented

by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1392] VGAM613 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM613 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM613 host target RNA into VGAM613 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1393] VGAM614 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM614 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM614 host target RNA into

VGAM614 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1394] It is appreciated that a function of VGR2855 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2855 gene include diagnosis, prevention and treatment of viral infection by Xestia C-nigrum Granulovirus. Specific functions, and accordingly utilities, of VGR2855 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2855 gene: VGAM613 host target protein and VGAM614 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM613 and VGAM614. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2856(VGR2856) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates ex-

pression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1395] VGR2856 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2856 gene was detected is described hereinabove with reference to Figs. 1-9.

[1396] VGR2856 gene encodes VGR2856 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1397] VGR2856 precursor RNA folds spatially, forming VGR2856 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2856 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2856 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1398] VGR2856 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM615 precursor RNA and VGAM616 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1399] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM615 RNA and VGAM616 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1400] VGAM615 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM615 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM615 host target RNA into VGAM615 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1401] VGAM616 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM616 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM616 host target RNA into VGAM616 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1402] It is appreciated that a function of VGR2856 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2856 gene include diagnosis, prevention and treatment of viral infection by Xestia C-nigrum Granulovirus. Specific functions, and accordingly utilities, of VGR2856 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in

the `operon-like` cluster of VGR2856 gene: VGAM615 host target protein and VGAM616 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM615 and VGAM616. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2857(VGR2857) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1403] VGR2857 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2857 gene was detected is described hereinabove with reference to Figs. 1-9.

[1404] VGR2857 gene encodes VGR2857 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1405] VGR2857 precursor RNA folds spatially, forming VGR2857

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2857 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2857 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1406] VGR2857 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM619 precursor RNA, VGAM620 precursor RNA, VGAM621 precursor RNA, VGAM622 precursor RNA, VGAM623 precursor RNA, VGAM624 precursor RNA, VGAM625 precursor RNA and VGAM626 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1407] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM619 RNA, VGAM620 RNA, VGAM621 RNA, VGAM622 RNA, VGAM623 RNA, VGAM624 RNA, VGAM625 RNA and VGAM626 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1408] VGAM619 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM619 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM619 host target RNA into VGAM619 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1409] VGAM620 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM620 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM620 host target RNA into VGAM620 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1410] VGAM621 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM621 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM621 host target RNA into VGAM621 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1411] VGAM622 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM622 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM622 host target RNA into VGAM622 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1412] VGAM623 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM623 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM623 host target RNA into VGAM623 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1413] VGAM624 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM624 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM624 host target RNA into VGAM624 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1414] VGAM625 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM625 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM625 host target RNA into VGAM625 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1415] VGAM626 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM626 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM626 host target RNA into VGAM626 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1416] It is appreciated that a function of VGR2857 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2857 gene include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus C. Specific functions, and accordingly utilities, of VGR2857 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2857 gene: VGAM619 host target protein, VGAM620 host target protein, VGAM621 host target protein, VGAM622 host target protein, VGAM623 host target protein, VGAM624 host target pro-

tein, VGAM625 host target protein and VGAM626 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM619, VGAM620, VGAM621, VGAM622, VGAM623, VGAM624, VGAM625 and VGAM626. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2858(VGR2858) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1417] VGR2858 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2858 gene was detected is described hereinabove with reference to Figs. 1-9.

[1418] VGR2858 gene encodes VGR2858 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1419] VGR2858 precursor RNA folds spatially, forming VGR2858

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2858 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2858 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1420] VGR2858 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM627 precursor RNA, VGAM628 precursor RNA, VGAM629 precursor RNA and VGAM630 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1421] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM627 RNA, VGAM628 RNA, VGAM629 RNA and VGAM630 RNA,

herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1422] VGAM627 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM627 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM627 host target RNA into VGAM627 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1423] VGAM628 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM628 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM628 host target RNA into VGAM628 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1424] VGAM629 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM629 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM629 host target RNA into VGAM629 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1425] VGAM630 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM630 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM630 host target RNA into VGAM630 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1426] It is appreciated that a function of VGR2858 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2858 gene include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus C. Specific functions, and accordingly utilities, of VGR2858 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2858 gene: VGAM627 host target protein, VGAM628 host target protein, VGAM629 host target protein and VGAM630 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM627, VGAM628, VGAM629 and VGAM630. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory vi-

ral gene, referred to here as Viral Genomic Record 2859(VGR2859) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1427] VGR2859 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2859 gene was detected is described hereinabove with reference to Figs. 1-9.

[1428] VGR2859 gene encodes VGR2859 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1429] VGR2859 precursor RNA folds spatially, forming VGR2859 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2859 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2859 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1430] VGR2859 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM631 precursor RNA and VGAM632 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1431] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM631 RNA and VGAM632 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1432] VGAM631 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM631 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM631 host target RNA into VGAM631 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1433] VGAM632 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM632 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM632 host target RNA into VGAM632 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1434] It is appreciated that a function of VGR2859 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2859 gene include diagnosis, prevention and treatment of viral infection by Ovine Astrovirus. Specific functions, and accordingly utili-

ties, of VGR2859 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2859 gene: VGAM631 host target protein and VGAM632 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM631 and VGAM632. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2860(VGR2860) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1435] VGR2860 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2860 gene was detected is described hereinabove with reference to Figs. 1-9.

[1436] VGR2860 gene encodes VGR2860 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[1437] VGR2860 precursor RNA folds spatially, forming VGR2860 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2860 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2860 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1438] VGR2860 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM633 precursor RNA and VGAM634 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1439] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM633

RNA and VGAM634 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1440] VGAM633 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM633 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM633 host target RNA into VGAM633 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1441] VGAM634 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM634 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM634 host target RNA into VGAM634 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1442] It is appreciated that a function of VGR2860 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2860 gene include diagnosis, prevention and treatment of viral infection by Turkey Astrovirus. Specific functions, and accordingly utilities, of VGR2860 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2860 gene: VGAM633 host target protein and VGAM634 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM633 and VGAM634. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2861(VGR2861) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1443] VGR2861 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2861 gene was detected is described hereinabove with reference to Figs. 1-9.

[1444] VGR2861 gene encodes VGR2861 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1445] VGR2861 precursor RNA folds spatially, forming VGR2861 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2861 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2861 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1446] VGR2861 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM635 precursor RNA and VGAM636 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1447] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM635 RNA and VGAM636 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1448] VGAM635 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM635 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM635 host target RNA into VGAM635 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1449] VGAM636 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM636 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM636 host target RNA into VGAM636 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1450] It is appreciated that a function of VGR2861 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2861 gene include diagnosis, prevention and treatment of viral infection by Cherry Mottle Leaf Virus. Specific functions, and accordingly utilities, of VGR2861 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2861 gene: VGAM635 host target protein and VGAM636 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM635 and VGAM636. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2862(VGR2862) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1451] VGR2862 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2862 gene was detected is described hereinabove with reference to Figs. 1-9.

[1452] VGR2862 gene encodes VGR2862 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1453] VGR2862 precursor RNA folds spatially, forming VGR2862 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2862 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2862 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1454] VGR2862 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM638 precursor RNA, VGAM639 precursor RNA and VGAM640 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1455] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM638 RNA, VGAM639 RNA and VGAM640 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA,

each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1456] VGAM638 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM638 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM638 host target RNA into VGAM638 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1457] VGAM639 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM639 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM639 host target RNA into

VGAM639 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1458] VGAM640 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM640 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM640 host target RNA into VGAM640 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1459] It is appreciated that a function of VGR2862 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2862 gene include diagnosis, prevention and treatment of viral infection by Turnip Mosaic Virus. Specific functions, and accordingly utilities, of VGR2862 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2862 gene: VGAM638 host
target protein, VGAM639 host target protein and
VGAM640 host target protein, herein schematically repre-
sented by VGAM1 HOST TARGET PROTEIN through VGAM3
HOST TARGET PROTEIN. The function of these host target
genes is elaborated hereinabove with reference to
VGAM638, VGAM639 and VGAM640. Fig. 9 further pro-
vides a conceptual description of novel bioinformatically
detected regulatory viral gene, referred to here as Viral
Genomic Record 2863(VGR2863) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[1460] VGR2863 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2863 gene was
detected is described hereinabove with reference to Figs.
1-9.

[1461] VGR2863 gene encodes VGR2863 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[1462] VGR2863 precursor RNA folds spatially, forming VGR2863 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2863 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2863 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1463] VGR2863 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM644 precursor RNA and VGAM645 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1464] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM644 RNA and VGAM645 RNA, herein schematically represented

by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1465] VGAM644 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM644 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM644 host target RNA into VGAM644 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1466] VGAM645 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM645 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM645 host target RNA into

VGAM645 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1467] It is appreciated that a function of VGR2863 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2863 gene include diagnosis, prevention and treatment of viral infection by Parvovirus H1. Specific functions, and accordingly utilities, of VGR2863 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2863 gene: VGAM644 host target protein and VGAM645 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM644 and VGAM645. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2864(VGR2864) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[1468] VGR2864 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2864 gene was detected is described hereinabove with reference to Figs. 1-9.

[1469] VGR2864 gene encodes VGR2864 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1470] VGR2864 precursor RNA folds spatially, forming VGR2864 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2864 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2864 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1471] VGR2864 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM647 precursor RNA, VGAM648 precursor RNA and VGAM649 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1472] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM647 RNA, VGAM648 RNA and VGAM649 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1473] VGAM647 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM647 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM647 host target RNA into

VGAM647 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1474] VGAM648 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM648 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM648 host target RNA into VGAM648 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1475] VGAM649 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM649 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM649 host target RNA into VGAM649 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1476] It is appreciated that a function of VGR2864 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2864 gene include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGR2864 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2864 gene: VGAM647 host target protein, VGAM648 host target protein and VGAM649 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM647, VGAM648 and VGAM649. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2865(VGR2865) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1477] VGR2865 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2865 gene was detected is described hereinabove with reference to Figs. 1-9.

[1478] VGR2865 gene encodes VGR2865 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1479] VGR2865 precursor RNA folds spatially, forming VGR2865 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2865 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2865 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1480] VGR2865 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM652 precursor RNA and VGAM653 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1481] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM652 RNA and VGAM653 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1482] VGAM652 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM652 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM652 host target RNA into

VGAM652 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1483] VGAM653 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM653 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM653 host target RNA into VGAM653 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1484] It is appreciated that a function of VGR2865 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2865 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2865 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2865 gene: VGAM652 host target protein and VGAM653 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM652 and VGAM653. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2866(VGR2866) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1485] VGR2866 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2866 gene was detected is described hereinabove with reference to Figs. 1-9.

[1486] VGR2866 gene encodes VGR2866 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1487] VGR2866 precursor RNA folds spatially, forming VGR2866

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2866 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2866 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1488] VGR2866 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM654 precursor RNA, VGAM655 precursor RNA, VGAM656 precursor RNA and VGAM657 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1489] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM654 RNA, VGAM655 RNA, VGAM656 RNA and VGAM657 RNA,

herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1490] VGAM654 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM654 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM654 host target RNA into VGAM654 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1491] VGAM655 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM655 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM655 host target RNA into VGAM655 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1492] VGAM656 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM656 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM656 host target RNA into VGAM656 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1493] VGAM657 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM657 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM657 host target RNA into VGAM657 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1494] It is appreciated that a function of VGR2866 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2866 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2866 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2866 gene: VGAM654 host target protein, VGAM655 host target protein, VGAM656 host target protein and VGAM657 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM654, VGAM655, VGAM656 and VGAM657. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory vi-

ral gene, referred to here as Viral Genomic Record 2867(VGR2867) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1495] VGR2867 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2867 gene was detected is described hereinabove with reference to Figs. 1-9.

[1496] VGR2867 gene encodes VGR2867 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1497] VGR2867 precursor RNA folds spatially, forming VGR2867 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2867 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2867 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1498] VGR2867 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM658 precursor RNA, VGAM659 precursor RNA and VGAM660 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1499] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM658 RNA, VGAM659 RNA and VGAM660 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1500] VGAM658 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM658 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM658 host target RNA into VGAM658 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1501] VGAM659 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM659 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM659 host target RNA into VGAM659 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1502] VGAM660 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM660 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM660 host target RNA into VGAM660 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1503] It is appreciated that a function of VGR2867 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2867 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2867 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2867 gene: VGAM658 host target protein, VGAM659 host target protein and VGAM660 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to

VGAM658, VGAM659 and VGAM660. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2868 (VGR2868) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1504] VGR2868 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2868 gene was detected is described hereinabove with reference to Figs. 1-9.

[1505] VGR2868 gene encodes VGR2868 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1506] VGR2868 precursor RNA folds spatially, forming VGR2868 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2868 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2868 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1507] VGR2868 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM663 precursor RNA, VGAM664 precursor RNA and VGAM665 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1508] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM663 RNA, VGAM664 RNA and VGAM665 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1509] VGAM663 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM663 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM663 host target RNA into VGAM663 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1510] VGAM664 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM664 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM664 host target RNA into VGAM664 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1511] VGAM665 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM665 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM665 host target RNA into VGAM665 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1512] It is appreciated that a function of VGR2868 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2868 gene include diagnosis, prevention and treatment of viral infection by Rachiplusia Ou Multiple Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR2868 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2868 gene: VGAM663 host target protein, VGAM664 host target protein and VGAM665 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN

through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM663, VGAM664 and VGAM665. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2869(VGR2869) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1513] VGR2869 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2869 gene was detected is described hereinabove with reference to Figs. 1-9.

[1514] VGR2869 gene encodes VGR2869 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1515] VGR2869 precursor RNA folds spatially, forming VGR2869 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2869 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2869 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1516] VGR2869 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM671 precursor RNA and VGAM672 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1517] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM671 RNA and VGAM672 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1518] VGAM671 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM671 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM671 host target RNA into VGAM671 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1519] VGAM672 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM672 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM672 host target RNA into VGAM672 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1520] It is appreciated that a function of VGR2869 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2869 gene include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGR2869 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2869 gene: VGAM671 host target protein and VGAM672 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM671 and VGAM672. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2870(VGR2870) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1521] VGR2870 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2870 gene was detected is described hereinabove with reference to Figs. 1–9.

[1522] VGR2870 gene encodes VGR2870 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1523] VGR2870 precursor RNA folds spatially, forming VGR2870 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2870 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2870 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1524] VGR2870 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM673 precursor RNA, VGAM674 precursor RNA, VGAM675 precursor RNA, VGAM676 precursor RNA, VGAM677 precursor RNA, VGAM678 precursor RNA, VGAM679 precursor RNA and VGAM680 precursor

RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1525] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM673 RNA, VGAM674 RNA, VGAM675 RNA, VGAM676 RNA, VGAM677 RNA, VGAM678 RNA, VGAM679 RNA and VGAM680 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1526] VGAM673 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM673 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM673 host target RNA into VGAM673 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1527] VGAM674 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM674 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM674 host target RNA into VGAM674 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1528] VGAM675 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM675 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM675 host target RNA into

VGAM675 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1529] VGAM676 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM676 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM676 host target RNA into VGAM676 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1530] VGAM677 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM677 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM677 host target RNA into VGAM677 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1531] VGAM678 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM678 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM678 host target RNA into VGAM678 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1532] VGAM679 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM679 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM679 host target RNA into VGAM679 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1533] VGAM680 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM680 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM680 host target RNA into VGAM680 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1534] It is appreciated that a function of VGR2870 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2870 gene include diagnosis, prevention and treatment of viral infection by Human Coronavirus 229E. Specific functions, and accord-

ingly utilities, of VGR2870 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2870 gene: VGAM673 host target protein, VGAM674 host target protein, VGAM675 host target protein, VGAM676 host target protein, VGAM677 host target protein, VGAM678 host target protein, VGAM679 host target protein and VGAM680 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM673, VGAM674, VGAM675, VGAM676, VGAM677, VGAM678, VGAM679 and VGAM680. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2871(VGR2871) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1535] VGR2871 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2871 gene was detected is described hereinabove with reference to Figs. 1–9.

[1536] VGR2871 gene encodes VGR2871 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1537] VGR2871 precursor RNA folds spatially, forming VGR2871 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2871 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2871 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1538] VGR2871 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM681 precursor RNA, VGAM682 precursor RNA, VGAM683 precursor RNA, VGAM684 precursor RNA, VGAM685 precursor RNA, VGAM686 precursor RNA, VGAM687 precursor RNA and VGAM688 precursor

RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1539] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM681 RNA, VGAM682 RNA, VGAM683 RNA, VGAM684 RNA, VGAM685 RNA, VGAM686 RNA, VGAM687 RNA and VGAM688 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1540] VGAM681 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM681 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM681 host target RNA into VGAM681 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1541] VGAM682 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM682 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM682 host target RNA into VGAM682 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1542] VGAM683 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM683 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM683 host target RNA into

VGAM683 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1543] VGAM684 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM684 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM684 host target RNA into VGAM684 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1544] VGAM685 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM685 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM685 host target RNA into VGAM685 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1545] VGAM686 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM686 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM686 host target RNA into VGAM686 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1546] VGAM687 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM687 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM687 host target RNA into VGAM687 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1547] VGAM688 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM688 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM688 host target RNA into VGAM688 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1548] It is appreciated that a function of VGR2871 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2871 gene include diagnosis, prevention and treatment of viral infection by Human Coronavirus 229E. Specific functions, and accord-

ingly utilities, of VGR2871 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2871 gene: VGAM681 host target protein, VGAM682 host target protein, VGAM683 host target protein, VGAM684 host target protein, VGAM685 host target protein, VGAM686 host target protein, VGAM687 host target protein and VGAM688 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM681, VGAM682, VGAM683, VGAM684, VGAM685, VGAM686, VGAM687 and VGAM688. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2872(VGR2872) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1549] VGR2872 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2872 gene was detected is described hereinabove with reference to Figs. 1-9.

[1550] VGR2872 gene encodes VGR2872 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1551] VGR2872 precursor RNA folds spatially, forming VGR2872 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2872 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2872 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1552] VGR2872 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM689 precursor RNA, VGAM690 precursor RNA, VGAM691 precursor RNA, VGAM692 precursor RNA, VGAM693 precursor RNA, VGAM694 precursor RNA, VGAM695 precursor RNA and VGAM696 precursor

RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1553] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM689 RNA, VGAM690 RNA, VGAM691 RNA, VGAM692 RNA, VGAM693 RNA, VGAM694 RNA, VGAM695 RNA and VGAM696 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1554] VGAM689 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM689 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM689 host target RNA into VGAM689 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1555] VGAM690 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM690 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM690 host target RNA into VGAM690 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1556] VGAM691 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM691 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM691 host target RNA into

VGAM691 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1557] VGAM692 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM692 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM692 host target RNA into VGAM692 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1558] VGAM693 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM693 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM693 host target RNA into VGAM693 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1559] VGAM694 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM694 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM694 host target RNA into VGAM694 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1560] VGAM695 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM695 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM695 host target RNA into VGAM695 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1561] VGAM696 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM696 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM696 host target RNA into VGAM696 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1562] It is appreciated that a function of VGR2872 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2872 gene include diagnosis, prevention and treatment of viral infection by Human Coronavirus 229E. Specific functions, and accord-

ingly utilities, of VGR2872 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2872 gene: VGAM689 host target protein, VGAM690 host target protein, VGAM691 host target protein, VGAM692 host target protein, VGAM693 host target protein, VGAM694 host target protein, VGAM695 host target protein and VGAM696 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM689, VGAM690, VGAM691, VGAM692, VGAM693, VGAM694, VGAM695 and VGAM696. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2873(VGR2873) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1563] VGR2873 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2873 gene was detected is described hereinabove with reference to Figs. 1-9.

[1564] VGR2873 gene encodes VGR2873 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1565] VGR2873 precursor RNA folds spatially, forming VGR2873 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2873 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2873 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1566] VGR2873 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM697 precursor RNA, VGAM698 precursor RNA, VGAM699 precursor RNA and VGAM700 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR,

each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1567] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM697 RNA, VGAM698 RNA, VGAM699 RNA and VGAM700 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1568] VGAM697 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM697 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM697 host target RNA into VGAM697 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1569] VGAM698 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM698 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM698 host target RNA into VGAM698 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1570] VGAM699 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM699 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM699 host target RNA into VGAM699 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1571] VGAM700 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM700 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM700 host target RNA into VGAM700 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1572] It is appreciated that a function of VGR2873 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2873 gene include diagnosis, prevention and treatment of viral infection by Human Coronavirus 229E. Specific functions, and accordingly utilities, of VGR2873 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2873 gene: VGAM697 host target protein, VGAM698 host target protein, VGAM699

host target protein and VGAM700 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM697, VGAM698, VGAM699 and VGAM700. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2874(VGR2874) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1573] VGR2874 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2874 gene was detected is described hereinabove with reference to Figs. 1–9.

[1574] VGR2874 gene encodes VGR2874 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1575] VGR2874 precursor RNA folds spatially, forming VGR2874 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2874 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2874 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1576] VGR2874 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM701 precursor RNA, VGAM702 precursor RNA, VGAM703 precursor RNA, VGAM704 precursor RNA, VGAM705 precursor RNA and VGAM706 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1577] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM701 RNA, VGAM702 RNA, VGAM703 RNA, VGAM704 RNA,

VGAM705 RNA and VGAM706 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1578] VGAM701 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM701 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM701 host target RNA into VGAM701 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1579] VGAM702 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM702 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM702 host target RNA into VGAM702 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1580] VGAM703 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM703 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM703 host target RNA into VGAM703 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1581] VGAM704 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM704 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM704 host target RNA into VGAM704 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1582] VGAM705 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM705 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM705 host target RNA into VGAM705 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1583] VGAM706 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM706 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM706 host target RNA into VGAM706 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1584] It is appreciated that a function of VGR2874 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2874 gene include diagnosis, prevention and treatment of viral infection by Human Coronavirus 229E. Specific functions, and accordingly utilities, of VGR2874 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2874 gene: VGAM701 host target protein, VGAM702 host target protein, VGAM703 host target protein, VGAM704 host target protein, VGAM705 host target protein and VGAM706 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM701, VGAM702,

VGAM703, VGAM704, VGAM705 and VGAM706. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2875 (VGR2875) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1585] VGR2875 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2875 gene was detected is described hereinabove with reference to Figs. 1-9.

[1586] VGR2875 gene encodes VGR2875 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1587] VGR2875 precursor RNA folds spatially, forming VGR2875 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2875 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2875 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1588] VGR2875 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM710 precursor RNA, VGAM711 precursor RNA and VGAM712 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1589] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM710 RNA, VGAM711 RNA and VGAM712 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1590] VGAM710 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM710 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM710 host target RNA into VGAM710 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1591] VGAM711 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM711 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM711 host target RNA into VGAM711 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1592] VGAM712 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM712 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM712 host target RNA into VGAM712 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1593] It is appreciated that a function of VGR2875 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2875 gene include diagnosis, prevention and treatment of viral infection by Pestivirus Type 2. Specific functions, and accordingly utilities, of VGR2875 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2875 gene: VGAM710 host target protein, VGAM711 host target protein and VGAM712 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM710, VGAM711 and VGAM712. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2876 (VGR2876) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1594] VGR2876 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2876 gene was detected is described hereinabove with reference to Figs. 1-9.

[1595] VGR2876 gene encodes VGR2876 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1596] VGR2876 precursor RNA folds spatially, forming VGR2876 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2876 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2876 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1597] VGR2876 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM713 precursor RNA and VGAM714 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1598] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM713 RNA and VGAM714 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1599] VGAM713 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM713 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM713 host target RNA into VGAM713 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1600] VGAM714 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM714 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM714 host target RNA into VGAM714 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1601] It is appreciated that a function of VGR2876 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2876 gene include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2876 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2876 gene: VGAM713 host target protein and VGAM714 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM713 and VGAM714. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2877(VGR2877) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1602] VGR2877 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2877 gene was detected is described hereinabove with reference to Figs. 1-9.

[1603] VGR2877 gene encodes VGR2877 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1604] VGR2877 precursor RNA folds spatially, forming VGR2877 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2877 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2877 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1605] VGR2877 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM715 precursor RNA, VGAM716 precursor RNA, VGAM717 precursor RNA and VGAM718 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR,

each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1606] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM715 RNA, VGAM716 RNA, VGAM717 RNA and VGAM718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1607] VGAM715 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM715 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM715 host target RNA into VGAM715 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1608] VGAM716 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM716 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM716 host target RNA into VGAM716 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1609] VGAM717 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM717 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM717 host target RNA into VGAM717 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1610] VGAM718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM718 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM718 host target RNA into VGAM718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1611] It is appreciated that a function of VGR2877 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2877 gene include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2877 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2877 gene: VGAM715 host target protein, VGAM716 host target protein,

VGAM717 host target protein and VGAM718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM715, VGAM716, VGAM717 and VGAM718. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2878(VGR2878) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1612] VGR2878 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2878 gene was detected is described hereinabove with reference to Figs. 1-9.

[1613] VGR2878 gene encodes VGR2878 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1614] VGR2878 precursor RNA folds spatially, forming VGR2878 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2878 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2878 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1615] VGR2878 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM719 precursor RNA and VGAM720 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1616] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM719 RNA and VGAM720 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1617] VGAM719 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM719 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM719 host target RNA into VGAM719 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1618] VGAM720 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM720 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM720 host target RNA into VGAM720 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1619] It is appreciated that a function of VGR2878 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2878 gene include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGR2878 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2878 gene: VGAM719 host target protein and VGAM720 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM719 and VGAM720. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2879(VGR2879) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in

the art.

[1620] VGR2879 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2879 gene was detected is described hereinabove with reference to Figs. 1-9.

[1621] VGR2879 gene encodes VGR2879 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1622] VGR2879 precursor RNA folds spatially, forming VGR2879 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2879 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2879 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1623] VGR2879 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM721 precursor RNA, VGAM722 pre-

cursor RNA, VGAM723 precursor RNA, VGAM724 precursor RNA and VGAM725 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1624] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM721 RNA, VGAM722 RNA, VGAM723 RNA, VGAM724 RNA and VGAM725 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1625] VGAM721 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM721 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM721 host target RNA into VGAM721 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1626] VGAM722 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM722 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM722 host target RNA into VGAM722 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1627] VGAM723 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM723 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM723 host target RNA into

VGAM723 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1628] VGAM724 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM724 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM724 host target RNA into VGAM724 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1629] VGAM725 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM725 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM725 host target RNA into VGAM725 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1630] It is appreciated that a function of VGR2879 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2879 gene include diagnosis, prevention and treatment of viral infection by Tomato Mosaic Virus. Specific functions, and accordingly utilities, of VGR2879 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2879 gene: VGAM721 host target protein, VGAM722 host target protein, VGAM723 host target protein, VGAM724 host target protein and VGAM725 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM721, VGAM722, VGAM723, VGAM724 and VGAM725. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene,

referred to here as Viral Genomic Record 2880(VGR2880) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1631] VGR2880 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2880 gene was detected is described hereinabove with reference to Figs. 1-9.

[1632] VGR2880 gene encodes VGR2880 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1633] VGR2880 precursor RNA folds spatially, forming VGR2880 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2880 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2880 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1634] VGR2880 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM727 precursor RNA and VGAM728 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1635] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM727 RNA and VGAM728 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1636] VGAM727 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM727 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM727 host target RNA into VGAM727 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1637] VGAM728 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM728 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM728 host target RNA into VGAM728 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1638] It is appreciated that a function of VGR2880 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2880 gene include diagnosis, prevention and treatment of viral infection by Aconitum Latent Virus. Specific functions, and accordingly

utilities, of VGR2880 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2880 gene: VGAM727 host target protein and VGAM728 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM727 and VGAM728. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2881(VGR2881) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1639] VGR2881 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2881 gene was detected is described hereinabove with reference to Figs. 1-9.

[1640] VGR2881 gene encodes VGR2881 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[1641] VGR2881 precursor RNA folds spatially, forming VGR2881 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2881 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2881 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1642] VGR2881 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM729 precursor RNA, VGAM730 precursor RNA, VGAM731 precursor RNA and VGAM732 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1643] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM729 RNA, VGAM730 RNA, VGAM731 RNA and VGAM732 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1644] VGAM729 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM729 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM729 host target RNA into VGAM729 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1645] VGAM730 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM730 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM730 host target RNA into VGAM730 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1646] VGAM731 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM731 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM731 host target RNA into VGAM731 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1647] VGAM732 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM732 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM732 host target RNA into VGAM732 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1648] It is appreciated that a function of VGR2881 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2881 gene include diagnosis, prevention and treatment of viral infection by Cydia Pomonella Granulovirus. Specific functions, and accordingly utilities, of VGR2881 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2881 gene: VGAM729 host target protein, VGAM730 host target protein, VGAM731 host target protein and VGAM732 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM729, VGAM730,

VGAM731 and VGAM732. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2882 (VGR2882) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1649] VGR2882 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2882 gene was detected is described hereinabove with reference to Figs. 1-9.

[1650] VGR2882 gene encodes VGR2882 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1651] VGR2882 precursor RNA folds spatially, forming VGR2882 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2882 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2882 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1652] VGR2882 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM733 precursor RNA, VGAM734 precursor RNA, VGAM735 precursor RNA, VGAM736 precursor RNA, VGAM737 precursor RNA and VGAM738 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1653] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM733 RNA, VGAM734 RNA, VGAM735 RNA, VGAM736 RNA, VGAM737 RNA and VGAM738 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1654] VGAM733 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM733 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM733 host target RNA into VGAM733 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1655] VGAM734 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM734 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM734 host target RNA into VGAM734 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1656] VGAM735 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM735 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM735 host target RNA into VGAM735 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1657] VGAM736 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM736 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM736 host target RNA into VGAM736 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1658] VGAM737 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM737 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM737 host target RNA into VGAM737 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1659] VGAM738 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM738 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM738 host target RNA into VGAM738 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1660] It is appreciated that a function of VGR2882 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2882 gene include diagnosis, prevention and treatment of viral infection by Barley Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGR2882 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2882 gene: VGAM733 host target protein, VGAM734 host target protein, VGAM735 host target protein, VGAM736 host target protein, VGAM737 host target protein and VGAM738 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM733, VGAM734, VGAM735, VGAM736, VGAM737 and VGAM738. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2883(VGR2883) viral gene, which encodes an `operon-like` cluster of

novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1661] VGR2883 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2883 gene was detected is described hereinabove with reference to Figs. 1-9.

[1662] VGR2883 gene encodes VGR2883 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1663] VGR2883 precursor RNA folds spatially, forming VGR2883 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2883 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2883 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1664] VGR2883 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM739 precursor RNA, VGAM740 precursor RNA, VGAM741 precursor RNA and VGAM742 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1665] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM739 RNA, VGAM740 RNA, VGAM741 RNA and VGAM742 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1666] VGAM739 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM739 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM739 host target RNA into VGAM739 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1667] VGAM740 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM740 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM740 host target RNA into VGAM740 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1668] VGAM741 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM741 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM741 host target RNA into VGAM741 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1669] VGAM742 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM742 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM742 host target RNA into VGAM742 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1670] It is appreciated that a function of VGR2883 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2883 gene include diagnosis, prevention and treatment of viral infection by

Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGR2883 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2883 gene: VGAM739 host target protein, VGAM740 host target protein, VGAM741 host target protein and VGAM742 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM739, VGAM740, VGAM741 and VGAM742. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2884(VGR2884) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1671] VGR2884 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2884 gene was detected is described hereinabove with reference to Figs.

1-9.

- [1672] VGR2884 gene encodes VGR2884 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1673] VGR2884 precursor RNA folds spatially, forming VGR2884 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2884 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2884 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1674] VGR2884 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM744 precursor RNA, VGAM745 precursor RNA, VGAM746 precursor RNA, VGAM747 precursor RNA, VGAM748 precursor RNA, VGAM749 precursor RNA, VGAM750 precursor RNA and VGAM751 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of

which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1675] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM744 RNA, VGAM745 RNA, VGAM746 RNA, VGAM747 RNA, VGAM748 RNA, VGAM749 RNA, VGAM750 RNA and VGAM751 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1676] VGAM744 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM744 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM744 host target RNA into VGAM744 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1677] VGAM745 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM745 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM745 host target RNA into VGAM745 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1678] VGAM746 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM746 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM746 host target RNA into VGAM746 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1679] VGAM747 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM747 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM747 host target RNA into VGAM747 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1680] VGAM748 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM748 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM748 host target RNA into VGAM748 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1681] VGAM749 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM749 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM749 host target RNA into VGAM749 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1682] VGAM750 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM750 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM750 host target RNA into

VGAM750 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1683] VGAM751 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM751 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM751 host target RNA into VGAM751 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1684] It is appreciated that a function of VGR2884 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2884 gene include diagnosis, prevention and treatment of viral infection by Bovine Coronavirus. Specific functions, and accordingly utilities, of VGR2884 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2884 gene: VGAM744 host
target protein, VGAM745 host target protein, VGAM746
host target protein, VGAM747 host target protein,
VGAM748 host target protein, VGAM749 host target pro-
tein, VGAM750 host target protein and VGAM751 host
target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM744,
VGAM745, VGAM746, VGAM747, VGAM748, VGAM749,
VGAM750 and VGAM751. Fig. 9 further provides a concep-
tual description of novel bioinformatically detected regu-
latory viral gene, referred to here as Viral Genomic Record
2885(VGR2885) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[1685] VGR2885 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2885 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [1686] VGR2885 gene encodes VGR2885 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1687] VGR2885 precursor RNA folds spatially, forming VGR2885 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2885 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2885 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1688] VGR2885 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM752 precursor RNA, VGAM753 precursor RNA, VGAM754 precursor RNA, VGAM755 precursor RNA, VGAM756 precursor RNA, VGAM757 precursor RNA, VGAM758 precursor RNA and VGAM759 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of

which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1689] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM752 RNA, VGAM753 RNA, VGAM754 RNA, VGAM755 RNA, VGAM756 RNA, VGAM757 RNA, VGAM758 RNA and VGAM759 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1690] VGAM752 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM752 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM752 host target RNA into VGAM752 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1691] VGAM753 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM753 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM753 host target RNA into VGAM753 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1692] VGAM754 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM754 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM754 host target RNA into VGAM754 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1693] VGAM755 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM755 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM755 host target RNA into VGAM755 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1694] VGAM756 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM756 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM756 host target RNA into VGAM756 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1695] VGAM757 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM757 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM757 host target RNA into VGAM757 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1696] VGAM758 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM758 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM758 host target RNA into

VGAM758 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1697] VGAM759 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM759 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM759 host target RNA into VGAM759 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1698] It is appreciated that a function of VGR2885 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2885 gene include diagnosis, prevention and treatment of viral infection by Bovine Coronavirus. Specific functions, and accordingly utilities, of VGR2885 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2885 gene: VGAM752 host
target protein, VGAM753 host target protein, VGAM754
host target protein, VGAM755 host target protein,
VGAM756 host target protein, VGAM757 host target pro-
tein, VGAM758 host target protein and VGAM759 host
target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM752,
VGAM753, VGAM754, VGAM755, VGAM756, VGAM757,
VGAM758 and VGAM759. Fig. 9 further provides a concep-
tual description of novel bioinformatically detected regu-
latory viral gene, referred to here as Viral Genomic Record
2886(VGR2886) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[1699] VGR2886 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2886 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [1700] VGR2886 gene encodes VGR2886 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1701] VGR2886 precursor RNA folds spatially, forming VGR2886 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2886 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2886 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1702] VGR2886 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM760 precursor RNA, VGAM761 precursor RNA, VGAM762 precursor RNA, VGAM763 precursor RNA, VGAM764 precursor RNA, VGAM765 precursor RNA, VGAM766 precursor RNA and VGAM767 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of

which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1703] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM760 RNA, VGAM761 RNA, VGAM762 RNA, VGAM763 RNA, VGAM764 RNA, VGAM765 RNA, VGAM766 RNA and VGAM767 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1704] VGAM760 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM760 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM760 host target RNA into VGAM760 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1705] VGAM761 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM761 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM761 host target RNA into VGAM761 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1706] VGAM762 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM762 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM762 host target RNA into VGAM762 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1707] VGAM763 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM763 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM763 host target RNA into VGAM763 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1708] VGAM764 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM764 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM764 host target RNA into VGAM764 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1709] VGAM765 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM765 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM765 host target RNA into VGAM765 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1710] VGAM766 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM766 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM766 host target RNA into

VGAM766 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1711] VGAM767 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM767 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM767 host target RNA into VGAM767 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1712] It is appreciated that a function of VGR2886 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2886 gene include diagnosis, prevention and treatment of viral infection by Bovine Coronavirus. Specific functions, and accordingly utilities, of VGR2886 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2886 gene: VGAM760 host
target protein, VGAM761 host target protein, VGAM762
host target protein, VGAM763 host target protein,
VGAM764 host target protein, VGAM765 host target pro-
tein, VGAM766 host target protein and VGAM767 host
target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM760,
VGAM761, VGAM762, VGAM763, VGAM764, VGAM765,
VGAM766 and VGAM767. Fig. 9 further provides a concep-
tual description of novel bioinformatically detected regu-
latory viral gene, referred to here as Viral Genomic Record
2887(VGR2887) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[1713] VGR2887 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2887 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [1714] VGR2887 gene encodes VGR2887 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1715] VGR2887 precursor RNA folds spatially, forming VGR2887 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2887 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2887 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1716] VGR2887 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM768 precursor RNA and VGAM769 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1717] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM768 RNA and VGAM769 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1718] VGAM768 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM768 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM768 host target RNA into VGAM768 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1719] VGAM769 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM769 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM769 host target RNA into VGAM769 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1720] It is appreciated that a function of VGR2887 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2887 gene include diagnosis, prevention and treatment of viral infection by Bovine Coronavirus. Specific functions, and accordingly utilities, of VGR2887 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2887 gene: VGAM768 host target protein and VGAM769 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM768 and VGAM769. Fig. 9 further provides a conceptual description of novel bioinformati-

cally detected regulatory viral gene, referred to here as Viral Genomic Record 2888(VGR2888) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1721] VGR2888 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2888 gene was detected is described hereinabove with reference to Figs. 1-9.

[1722] VGR2888 gene encodes VGR2888 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1723] VGR2888 precursor RNA folds spatially, forming VGR2888 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2888 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2888 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1724] VGR2888 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM771 precursor RNA, VGAM772 precursor RNA, VGAM773 precursor RNA, VGAM774 precursor RNA and VGAM775 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1725] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM771 RNA, VGAM772 RNA, VGAM773 RNA, VGAM774 RNA and VGAM775 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1726] VGAM771 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM771 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM771 host target RNA into VGAM771 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1727] VGAM772 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM772 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM772 host target RNA into VGAM772 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1728] VGAM773 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM773 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM773 host target RNA into VGAM773 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1729] VGAM774 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM774 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM774 host target RNA into VGAM774 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1730] VGAM775 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM775 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM775 host target RNA into VGAM775 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1731] It is appreciated that a function of VGR2888 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2888 gene include diagnosis, prevention and treatment of viral infection by Bovine Coronavirus. Specific functions, and accordingly utilities, of VGR2888 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2888 gene: VGAM771 host target protein, VGAM772 host target protein, VGAM773 host target protein, VGAM774 host target protein and VGAM775 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM771, VGAM772, VGAM773, VGAM774 and VGAM775. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2889 (VGR2889) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1732] VGR2889 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2889 gene was detected is described hereinabove with reference to Figs. 1-9.

[1733] VGR2889 gene encodes VGR2889 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1734] VGR2889 precursor RNA folds spatially, forming VGR2889 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2889 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2889 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1735] VGR2889 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM781 precursor RNA, VGAM782 precursor RNA, VGAM783 precursor RNA and VGAM784 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1736] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM781 RNA, VGAM782 RNA, VGAM783 RNA and VGAM784 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1737] VGAM781 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM781 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM781 host target RNA into VGAM781 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1738] VGAM782 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM782 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM782 host target RNA into VGAM782 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1739] VGAM783 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM783 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM783 host target RNA into VGAM783 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1740] VGAM784 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM784 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM784 host target RNA into VGAM784 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1741] It is appreciated that a function of VGR2889 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2889 gene include diagnosis, prevention and treatment of viral infection by Deer Tick Virus. Specific functions, and accordingly utilities, of VGR2889 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2889 gene: VGAM781 host target protein, VGAM782 host target protein, VGAM783 host target protein and VGAM784 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM781, VGAM782, VGAM783 and VGAM784. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2890(VGR2890) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1742] VGR2890 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2890 gene was detected is described hereinabove with reference to Figs. 1-9.

[1743] VGR2890 gene encodes VGR2890 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1744] VGR2890 precursor RNA folds spatially, forming VGR2890 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2890 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2890 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1745] VGR2890 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM785 precursor RNA, VGAM786 precursor RNA, VGAM787 precursor RNA and VGAM788 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1746] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM785 RNA, VGAM786 RNA, VGAM787 RNA and VGAM788 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1747] VGAM785 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM785 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM785 host target RNA into VGAM785 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1748] VGAM786 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM786 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM786 host target RNA into VGAM786 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1749] VGAM787 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM787 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM787 host target RNA into VGAM787 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1750] VGAM788 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM788 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM788 host target RNA into VGAM788 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1751] It is appreciated that a function of VGR2890 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2890 gene include diagnosis, prevention and treatment of viral infection by Zucchini Yellow Mosaic Virus. Specific functions, and ac-

cordingly utilities, of VGR2890 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2890 gene: VGAM785 host target protein, VGAM786 host target protein, VGAM787 host target protein and VGAM788 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM785, VGAM786, VGAM787 and VGAM788. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2891(VGR2891) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1752] VGR2891 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2891 gene was detected is described hereinabove with reference to Figs. 1-9.

- [1753] VGR2891 gene encodes VGR2891 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1754] VGR2891 precursor RNA folds spatially, forming VGR2891 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2891 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2891 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1755] VGR2891 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM789 precursor RNA, VGAM790 precursor RNA and VGAM791 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [1756] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM789 RNA, VGAM790 RNA and VGAM791 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [1757] VGAM789 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM789 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM789 host target RNA into VGAM789 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [1758] VGAM790 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM790 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM790 host target RNA into VGAM790 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1759] VGAM791 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM791 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM791 host target RNA into VGAM791 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1760] It is appreciated that a function of VGR2891 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2891 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2891 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2891 gene: VGAM789 host target protein, VGAM790 host target protein and VGAM791 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM789, VGAM790 and VGAM791. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2892(VGR2892) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1761] VGR2892 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2892 gene was detected is described hereinabove with reference to Figs. 1-9.

[1762] VGR2892 gene encodes VGR2892 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1763] VGR2892 precursor RNA folds spatially, forming VGR2892 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2892 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2892 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1764] VGR2892 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM792 precursor RNA and VGAM793 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1765] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM792 RNA and VGAM793 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1766] VGAM792 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM792 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM792 host target RNA into VGAM792 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1767] VGAM793 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM793 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM793 host target RNA into VGAM793 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1768] It is appreciated that a function of VGR2892 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2892 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2892 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2892 gene: VGAM792 host target protein and VGAM793 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target

genes is elaborated hereinabove with reference to VGAM792 and VGAM793. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2893 (VGR2893) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1769] VGR2893 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2893 gene was detected is described hereinabove with reference to Figs. 1-9.

[1770] VGR2893 gene encodes VGR2893 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1771] VGR2893 precursor RNA folds spatially, forming VGR2893 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2893 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2893 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1772] VGR2893 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM795 precursor RNA and VGAM796 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1773] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM795 RNA and VGAM796 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1774] VGAM795 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM795 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM795 host target RNA into VGAM795 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1775] VGAM796 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM796 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM796 host target RNA into VGAM796 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1776] It is appreciated that a function of VGR2893 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2893 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2893 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2893 gene: VGAM795 host target protein and VGAM796 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM795 and VGAM796. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2894(VGR2894) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1777] VGR2894 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2894 gene was

detected is described hereinabove with reference to Figs. 1-9.

[1778] VGR2894 gene encodes VGR2894 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1779] VGR2894 precursor RNA folds spatially, forming VGR2894 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2894 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2894 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1780] VGR2894 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM797 precursor RNA and VGAM798 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM

FOLDED PRECURSOR RNA of Fig. 1.

- [1781] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM797 RNA and VGAM798 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [1782] VGAM797 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM797 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM797 host target RNA into VGAM797 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [1783] VGAM798 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM798 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM798 host target RNA into VGAM798 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1784] It is appreciated that a function of VGR2894 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2894 gene include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2894 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2894 gene: VGAM797 host target protein and VGAM798 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to

VGAM797 and VGAM798. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2895 (VGR2895) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1785] VGR2895 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2895 gene was detected is described hereinabove with reference to Figs. 1-9.

[1786] VGR2895 gene encodes VGR2895 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1787] VGR2895 precursor RNA folds spatially, forming VGR2895 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2895 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2895 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1788] VGR2895 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM799 precursor RNA and VGAM800 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1789] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM799 RNA and VGAM800 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1790] VGAM799 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM799 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM799 host target RNA into VGAM799 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1791] VGAM800 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM800 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM800 host target RNA into VGAM800 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1792] It is appreciated that a function of VGR2895 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2895 gene include

diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGR2895 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2895 gene: VGAM799 host target protein and VGAM800 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM799 and VGAM800. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2896(VGR2896) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1793] VGR2896 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2896 gene was detected is described hereinabove with reference to Figs.

1-9.

[1794] VGR2896 gene encodes VGR2896 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1795] VGR2896 precursor RNA folds spatially, forming VGR2896 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2896 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2896 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1796] VGR2896 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM801 precursor RNA, VGAM802 precursor RNA and VGAM803 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[1797] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM801 RNA, VGAM802 RNA and VGAM803 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1798] VGAM801 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM801 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM801 host target RNA into VGAM801 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1799] VGAM802 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM802 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM802 host target RNA into VGAM802 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1800] VGAM803 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM803 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM803 host target RNA into VGAM803 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1801] It is appreciated that a function of VGR2896 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2896 gene include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2896 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2896 gene: VGAM801 host target protein, VGAM802 host target protein and VGAM803 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM801, VGAM802 and VGAM803. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2897(VGR2897) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1802] VGR2897 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2897 gene was detected is described hereinabove with reference to Figs. 1-9.

[1803] VGR2897 gene encodes VGR2897 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1804] VGR2897 precursor RNA folds spatially, forming VGR2897 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2897 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2897 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1805] VGR2897 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM807 precursor RNA, VGAM808 precursor RNA and VGAM809 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1806] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM807 RNA, VGAM808 RNA and VGAM809 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1807] VGAM807 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM807 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM807 host target RNA into VGAM807 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1808] VGAM808 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM808 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM808 host target RNA into VGAM808 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1809] VGAM809 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM809 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM809 host target RNA into VGAM809 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1810] It is appreciated that a function of VGR2897 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2897 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2897 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2897 gene: VGAM807 host target protein, VGAM808 host target protein and VGAM809 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM807, VGAM808 and VGAM809. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2898(VGR2898) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1811] VGR2898 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2898 gene was detected is described hereinabove with reference to Figs. 1-9.

[1812] VGR2898 gene encodes VGR2898 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1813] VGR2898 precursor RNA folds spatially, forming VGR2898 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2898 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2898 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1814] VGR2898 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM812 precursor RNA, VGAM813 precursor RNA and VGAM814 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1815] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM812 RNA, VGAM813 RNA and VGAM814 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1816] VGAM812 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM812 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM812 host target RNA into VGAM812 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1817] VGAM813 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM813 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM813 host target RNA into VGAM813 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1818] VGAM814 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM814 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM814 host target RNA into VGAM814 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1819] It is appreciated that a function of VGR2898 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2898 gene include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2898 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2898 gene: VGAM812 host target protein, VGAM813 host target protein and VGAM814 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM812, VGAM813 and VGAM814. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2899(VGR2899) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1820] VGR2899 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2899 gene was detected is described hereinabove with reference to Figs. 1-9.

[1821] VGR2899 gene encodes VGR2899 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1822] VGR2899 precursor RNA folds spatially, forming VGR2899 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2899 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2899 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1823] VGR2899 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM

precursor RNAs, VGAM815 precursor RNA and VGAM816 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1824] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM815 RNA and VGAM816 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1825] VGAM815 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM815 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM815 host target RNA into VGAM815 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1826] VGAM816 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM816 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM816 host target RNA into VGAM816 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1827] It is appreciated that a function of VGR2899 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2899 gene include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGR2899 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2899 gene: VGAM815

host target protein and VGAM816 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM815 and VGAM816. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2900(VGR2900) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1828] VGR2900 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2900 gene was detected is described hereinabove with reference to Figs. 1–9.

[1829] VGR2900 gene encodes VGR2900 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1830] VGR2900 precursor RNA folds spatially, forming VGR2900 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2900 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2900 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1831] VGR2900 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM821 precursor RNA and VGAM822 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1832] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM821 RNA and VGAM822 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1833] VGAM821 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM821 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM821 host target RNA into VGAM821 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1834] VGAM822 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM822 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM822 host target RNA into VGAM822 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1835] It is appreciated that a function of VGR2900 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2900 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGR2900 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2900 gene: VGAM821 host target protein and VGAM822 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM821 and VGAM822. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2901(VGR2901) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1836] VGR2901 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2901 gene was detected is described hereinabove with reference to Figs. 1-9.

[1837] VGR2901 gene encodes VGR2901 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1838] VGR2901 precursor RNA folds spatially, forming VGR2901 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2901 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2901 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1839] VGR2901 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM823 precursor RNA and VGAM824 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1840] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM823 RNA and VGAM824 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1841] VGAM823 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM823 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM823 host target RNA into VGAM823 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1842] VGAM824 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM824 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM824 host target RNA into VGAM824 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1843] It is appreciated that a function of VGR2901 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2901 gene include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGR2901 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2901 gene: VGAM823 host target protein and VGAM824 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM823 and VGAM824. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2902 (VGR2902) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1844] VGR2902 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2902 gene was detected is described hereinabove with reference to Figs. 1-9.

[1845] VGR2902 gene encodes VGR2902 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1846] VGR2902 precursor RNA folds spatially, forming VGR2902 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2902 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2902 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1847] VGR2902 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM826 precursor RNA and VGAM827 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1848] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM826 RNA and VGAM827 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1849] VGAM826 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM826 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM826 host target RNA into VGAM826 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1850] VGAM827 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM827 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM827 host target RNA into VGAM827 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1851] It is appreciated that a function of VGR2902 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2902 gene include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2902 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2902 gene: VGAM826 host target protein and VGAM827 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM826 and VGAM827. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2903(VGR2903) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1852] VGR2903 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2903 gene was

detected is described hereinabove with reference to Figs. 1-9.

[1853] VGR2903 gene encodes VGR2903 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1854] VGR2903 precursor RNA folds spatially, forming VGR2903 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2903 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2903 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1855] VGR2903 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM828 precursor RNA, VGAM829 precursor RNA and VGAM830 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1856] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM828 RNA, VGAM829 RNA and VGAM830 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1857] VGAM828 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM828 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM828 host target RNA into VGAM828 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1858] VGAM829 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM829 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM829 host target RNA into VGAM829 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1859] VGAM830 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM830 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM830 host target RNA into VGAM830 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1860] It is appreciated that a function of VGR2903 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2903 gene include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGR2903 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2903 gene: VGAM828 host target protein, VGAM829 host target protein and VGAM830 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM828, VGAM829 and VGAM830. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2904(VGR2904) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1861] VGR2904 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2904 gene was detected is described hereinabove with reference to Figs. 1-9.

[1862] VGR2904 gene encodes VGR2904 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1863] VGR2904 precursor RNA folds spatially, forming VGR2904 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2904 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2904 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1864] VGR2904 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM831 precursor RNA and VGAM832 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1865] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM831 RNA and VGAM832 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1866] VGAM831 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM831 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM831 host target RNA into VGAM831 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1867] VGAM832 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM832 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM832 host target RNA into VGAM832 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1868] It is appreciated that a function of VGR2904 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2904 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6B. Specific functions, and accordingly utilities, of VGR2904 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2904 gene: VGAM831 host target protein and VGAM832 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM831 and VGAM832. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2905 (VGR2905) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1869] VGR2905 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2905 gene was detected is described hereinabove with reference to Figs. 1-9.

[1870] VGR2905 gene encodes VGR2905 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1871] VGR2905 precursor RNA folds spatially, forming VGR2905 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2905 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2905 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1872] VGR2905 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM833 precursor RNA, VGAM834 precursor RNA, VGAM835 precursor RNA, VGAM836 precursor RNA, VGAM837 precursor RNA and VGAM838 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1873] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM833 RNA, VGAM834 RNA, VGAM835 RNA, VGAM836 RNA, VGAM837 RNA and VGAM838 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1874] VGAM833 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM833 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM833 host target RNA into VGAM833 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1875] VGAM834 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM834 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM834 host target RNA into VGAM834 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1876] VGAM835 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM835 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM835 host target RNA into VGAM835 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1877] VGAM836 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM836 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM836 host target RNA into VGAM836 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[1878] VGAM837 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM837 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM837 host target RNA into VGAM837 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1879] VGAM838 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM838 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM838 host target RNA into VGAM838 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1880] It is appreciated that a function of VGR2905 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2905 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR2905 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2905 gene: VGAM833 host target protein, VGAM834 host target protein, VGAM835 host target protein, VGAM836 host target protein, VGAM837 host target protein and VGAM838 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM833, VGAM834, VGAM835, VGAM836, VGAM837 and VGAM838. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2906(VGR2906) viral gene, which

encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1881] VGR2906 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2906 gene was detected is described hereinabove with reference to Figs. 1-9.

[1882] VGR2906 gene encodes VGR2906 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1883] VGR2906 precursor RNA folds spatially, forming VGR2906 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2906 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2906 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[1884] VGR2906 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM841 precursor RNA and VGAM842 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1885] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM841 RNA and VGAM842 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1886] VGAM841 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM841 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM841 host target RNA into VGAM841 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1887] VGAM842 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM842 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM842 host target RNA into VGAM842 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1888] It is appreciated that a function of VGR2906 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2906 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2906 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2906 gene: VGAM841 host target protein and VGAM842 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM841 and VGAM842. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2907(VGR2907) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1889] VGR2907 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2907 gene was detected is described hereinabove with reference to Figs. 1-9.

[1890] VGR2907 gene encodes VGR2907 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1891] VGR2907 precursor RNA folds spatially, forming VGR2907 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2907 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2907 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1892] VGR2907 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM843 precursor RNA and VGAM844 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1893] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM843 RNA and VGAM844 RNA, herein schematically represented

by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1894] VGAM843 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM843 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM843 host target RNA into VGAM843 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1895] VGAM844 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM844 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM844 host target RNA into

VGAM844 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1896] It is appreciated that a function of VGR2907 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2907 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR2907 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2907 gene: VGAM843 host target protein and VGAM844 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM843 and VGAM844. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2908(VGR2908) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1897] VGR2908 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2908 gene was detected is described hereinabove with reference to Figs. 1-9.

[1898] VGR2908 gene encodes VGR2908 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1899] VGR2908 precursor RNA folds spatially, forming VGR2908 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2908 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2908 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1900] VGR2908 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM

precursor RNAs, VGAM845 precursor RNA, VGAM846 precursor RNA, VGAM847 precursor RNA and VGAM848 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1901] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM845 RNA, VGAM846 RNA, VGAM847 RNA and VGAM848 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1902] VGAM845 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM845 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM845 host target RNA into

VGAM845 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1903] VGAM846 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM846 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM846 host target RNA into VGAM846 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1904] VGAM847 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM847 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM847 host target RNA into VGAM847 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1905] VGAM848 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM848 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM848 host target RNA into VGAM848 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1906] It is appreciated that a function of VGR2908 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2908 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2908 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2908 gene: VGAM845 host target protein, VGAM846 host target protein, VGAM847 host target protein and VGAM848 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM845, VGAM846, VGAM847 and VGAM848. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2909(VGR2909) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1907] VGR2909 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2909 gene was detected is described hereinabove with reference to Figs. 1-9.

[1908] VGR2909 gene encodes VGR2909 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1909] VGR2909 precursor RNA folds spatially, forming VGR2909 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2909 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2909 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1910] VGR2909 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM849 precursor RNA, VGAM850 precursor RNA and VGAM851 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1911] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM849 RNA, VGAM850 RNA and VGAM851 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1912] VGAM849 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM849 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM849 host target RNA into VGAM849 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1913] VGAM850 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM850 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM850 host target RNA into VGAM850 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1914] VGAM851 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM851 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM851 host target RNA into VGAM851 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1915] It is appreciated that a function of VGR2909 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2909 gene include

diagnosis, prevention and treatment of viral infection by Lymphocystis Disease Virus 1. Specific functions, and accordingly utilities, of VGR2909 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2909 gene: VGAM849 host target protein, VGAM850 host target protein and VGAM851 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM849, VGAM850 and VGAM851. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2910(VGR2910) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1916] VGR2910 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2910 gene was detected is described hereinabove with reference to Figs.

1-9.

- [1917] VGR2910 gene encodes VGR2910 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [1918] VGR2910 precursor RNA folds spatially, forming VGR2910 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2910 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2910 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [1919] VGR2910 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM855 precursor RNA and VGAM856 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1920] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM855 RNA and VGAM856 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1921] VGAM855 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM855 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM855 host target RNA into VGAM855 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1922] VGAM856 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM856 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM856 host target RNA into VGAM856 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1923] It is appreciated that a function of VGR2910 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2910 gene include diagnosis, prevention and treatment of viral infection by African Swine Fever Virus. Specific functions, and accordingly utilities, of VGR2910 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2910 gene: VGAM855 host target protein and VGAM856 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM855 and VGAM856. Fig. 9 further provides a conceptual description of novel bioinformati-

cally detected regulatory viral gene, referred to here as Viral Genomic Record 2911(VGR2911) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1924] VGR2911 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2911 gene was detected is described hereinabove with reference to Figs. 1-9.

[1925] VGR2911 gene encodes VGR2911 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1926] VGR2911 precursor RNA folds spatially, forming VGR2911 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2911 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2911 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[1927] VGR2911 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM857 precursor RNA, VGAM858 precursor RNA and VGAM859 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1928] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM857 RNA, VGAM858 RNA and VGAM859 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1929] VGAM857 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM857 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM857 host target RNA into VGAM857 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1930] VGAM858 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM858 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM858 host target RNA into VGAM858 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1931] VGAM859 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM859 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM859 host target RNA into VGAM859 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1932] It is appreciated that a function of VGR2911 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2911 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR2911 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2911 gene: VGAM857 host target protein, VGAM858 host target protein and VGAM859 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to

VGAM857, VGAM858 and VGAM859. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2912 (VGR2912) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1933] VGR2912 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2912 gene was detected is described hereinabove with reference to Figs. 1-9.

[1934] VGR2912 gene encodes VGR2912 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1935] VGR2912 precursor RNA folds spatially, forming VGR2912 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2912 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2912 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1936] VGR2912 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM861 precursor RNA, VGAM862 precursor RNA, VGAM863 precursor RNA and VGAM864 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1937] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM861 RNA, VGAM862 RNA, VGAM863 RNA and VGAM864 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1938] VGAM861 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM861 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM861 host target RNA into VGAM861 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1939] VGAM862 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM862 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM862 host target RNA into VGAM862 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1940] VGAM863 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM863 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM863 host target RNA into VGAM863 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1941] VGAM864 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM864 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM864 host target RNA into VGAM864 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1942] It is appreciated that a function of VGR2912 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2912 gene include diagnosis, prevention and treatment of viral infection by Ictalurid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2912 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2912 gene: VGAM861 host target protein, VGAM862 host target protein, VGAM863 host target protein and VGAM864 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM861, VGAM862, VGAM863 and VGAM864. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2913(VGR2913) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1943] VGR2913 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2913 gene was detected is described hereinabove with reference to Figs. 1–9.

[1944] VGR2913 gene encodes VGR2913 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1945] VGR2913 precursor RNA folds spatially, forming VGR2913 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2913 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2913 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[1946] VGR2913 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM865 precursor RNA and VGAM866 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1947] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM865 RNA and VGAM866 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1948] VGAM865 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM865 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM865 host target RNA into VGAM865 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1949] VGAM866 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM866 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM866 host target RNA into VGAM866 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1950] It is appreciated that a function of VGR2913 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2913 gene include diagnosis, prevention and treatment of viral infection by Swinepox Virus. Specific functions, and accordingly utilities, of VGR2913 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2913 gene: VGAM865 host target protein and VGAM866 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM865 and VGAM866. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2914 (VGR2914) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1951] VGR2914 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2914 gene was detected is described hereinabove with reference to Figs. 1-9.

[1952] VGR2914 gene encodes VGR2914 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1953] VGR2914 precursor RNA folds spatially, forming VGR2914 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2914 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2914 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1954] VGR2914 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM867 precursor RNA and VGAM868 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1955] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM867 RNA and VGAM868 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1956] VGAM867 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM867 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM867 host target RNA into VGAM867 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1957] VGAM868 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM868 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM868 host target RNA into VGAM868 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1958] It is appreciated that a function of VGR2914 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2914 gene include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGR2914 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2914 gene: VGAM867 host target protein and VGAM868 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM867 and VGAM868. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2915(VGR2915) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1959] VGR2915 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2915 gene was

detected is described hereinabove with reference to Figs. 1–9.

[1960] VGR2915 gene encodes VGR2915 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1961] VGR2915 precursor RNA folds spatially, forming VGR2915 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2915 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2915 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1962] VGR2915 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM869 precursor RNA, VGAM870 precursor RNA, VGAM871 precursor RNA, VGAM872 precursor RNA and VGAM873 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor

sor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1963] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM869 RNA, VGAM870 RNA, VGAM871 RNA, VGAM872 RNA and VGAM873 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1964] VGAM869 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM869 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM869 host target RNA into VGAM869 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1965] VGAM870 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM870 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM870 host target RNA into VGAM870 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1966] VGAM871 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM871 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM871 host target RNA into VGAM871 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1967] VGAM872 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM872 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM872 host target RNA into VGAM872 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1968] VGAM873 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM873 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM873 host target RNA into VGAM873 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1969] It is appreciated that a function of VGR2915 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2915 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2915 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2915 gene: VGAM869 host target protein, VGAM870 host target protein, VGAM871 host target protein, VGAM872 host target protein and VGAM873 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM869, VGAM870, VGAM871, VGAM872 and VGAM873. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2916(VGR2916) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the

function and utility of which at least one host target gene is known in the art.

[1970] VGR2916 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2916 gene was detected is described hereinabove with reference to Figs. 1-9.

[1971] VGR2916 gene encodes VGR2916 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1972] VGR2916 precursor RNA folds spatially, forming VGR2916 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2916 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2916 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1973] VGR2916 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM875 precursor RNA, VGAM876 precursor RNA and VGAM877 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1974] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM875 RNA, VGAM876 RNA and VGAM877 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1975] VGAM875 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM875 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM875 host target RNA into

VGAM875 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1976] VGAM876 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM876 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM876 host target RNA into VGAM876 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1977] VGAM877 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM877 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM877 host target RNA into VGAM877 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1978] It is appreciated that a function of VGR2916 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2916 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGR2916 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2916 gene: VGAM875 host target protein, VGAM876 host target protein and VGAM877 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM875, VGAM876 and VGAM877. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2917(VGR2917) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[1979] VGR2917 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2917 gene was detected is described hereinabove with reference to Figs. 1-9.

[1980] VGR2917 gene encodes VGR2917 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1981] VGR2917 precursor RNA folds spatially, forming VGR2917 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2917 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2917 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1982] VGR2917 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM880 precursor RNA and VGAM881 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1983] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM880 RNA and VGAM881 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[1984] VGAM880 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM880 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM880 host target RNA into

VGAM880 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1985] VGAM881 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM881 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM881 host target RNA into VGAM881 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1986] It is appreciated that a function of VGR2917 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2917 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 3. Specific functions, and accordingly utilities, of VGR2917 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2917 gene: VGAM880 host
target protein and VGAM881 host target protein, herein
schematically represented by VGAM1 HOST TARGET PRO-
TEIN through VGAM3 HOST TARGET PROTEIN. The func-
tion of these host target genes is elaborated hereinabove
with reference to VGAM880 and VGAM881. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 2918(VGR2918) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[1987] VGR2918 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2918 gene was
detected is described hereinabove with reference to Figs.
1-9.

[1988] VGR2918 gene encodes VGR2918 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[1989] VGR2918 precursor RNA folds spatially, forming VGR2918

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2918 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2918 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1990] VGR2918 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM886 precursor RNA and VGAM887 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1991] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM886 RNA and VGAM887 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[1992] VGAM886 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM886 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM886 host target RNA into VGAM886 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1993] VGAM887 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM887 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM887 host target RNA into VGAM887 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[1994] It is appreciated that a function of VGR2918 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2918 gene include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGR2918 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2918 gene: VGAM886 host target protein and VGAM887 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM886 and VGAM887. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2919(VGR2919) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least

one host target gene is known in the art.

[1995] VGR2919 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2919 gene was detected is described hereinabove with reference to Figs. 1-9.

[1996] VGR2919 gene encodes VGR2919 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[1997] VGR2919 precursor RNA folds spatially, forming VGR2919 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2919 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2919 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[1998] VGR2919 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM888 precursor RNA, VGAM889 pre-

cursor RNA, VGAM890 precursor RNA and VGAM891 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[1999] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM888 RNA, VGAM889 RNA, VGAM890 RNA and VGAM891 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2000] VGAM888 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM888 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM888 host target RNA into VGAM888 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2001] VGAM889 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM889 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM889 host target RNA into VGAM889 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2002] VGAM890 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM890 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM890 host target RNA into

VGAM890 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2003] VGAM891 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM891 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM891 host target RNA into VGAM891 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2004] It is appreciated that a function of VGR2919 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2919 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2919 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2919 gene: VGAM888 host
target protein, VGAM889 host target protein, VGAM890
host target protein and VGAM891 host target protein,
herein schematically represented by VGAM1 HOST TARGET
PROTEIN through VGAM3 HOST TARGET PROTEIN. The
function of these host target genes is elaborated herein-
above with reference to VGAM888, VGAM889, VGAM890
and VGAM891. Fig. 9 further provides a conceptual de-
scription of novel bioinformatically detected regulatory vi-
ral gene, referred to here as Viral Genomic Record
2920(VGR2920) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[2005] VGR2920 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2920 gene was
detected is described hereinabove with reference to Figs.
1-9.

[2006] VGR2920 gene encodes VGR2920 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2007] VGR2920 precursor RNA folds spatially, forming VGR2920 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2920 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2920 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2008] VGR2920 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM892 precursor RNA, VGAM893 precursor RNA and VGAM894 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2009] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM892 RNA, VGAM893 RNA and VGAM894 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2010] VGAM892 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM892 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM892 host target RNA into VGAM892 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2011] VGAM893 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM893 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM893 host target RNA into VGAM893 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2012] VGAM894 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM894 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM894 host target RNA into VGAM894 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2013] It is appreciated that a function of VGR2920 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2920 gene include diagnosis, prevention and treatment of viral infection by

Periplaneta Fuliginosa Densovirus. Specific functions, and accordingly utilities, of VGR2920 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2920 gene: VGAM892 host target protein, VGAM893 host target protein and VGAM894 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM892, VGAM893 and VGAM894. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2921(VGR2921) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2014] VGR2921 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2921 gene was detected is described hereinabove with reference to Figs. 1-9.

- [2015] VGR2921 gene encodes VGR2921 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2016] VGR2921 precursor RNA folds spatially, forming VGR2921 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2921 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2921 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2017] VGR2921 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM895 precursor RNA, VGAM896 precursor RNA and VGAM897 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2018] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM895 RNA, VGAM896 RNA and VGAM897 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2019] VGAM895 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM895 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM895 host target RNA into VGAM895 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2020] VGAM896 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM896 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM896 host target RNA into VGAM896 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2021] VGAM897 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM897 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM897 host target RNA into VGAM897 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2022] It is appreciated that a function of VGR2921 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2921 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2921 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2921 gene: VGAM895 host target protein, VGAM896 host target protein and VGAM897 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM895, VGAM896 and VGAM897. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2922(VGR2922) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2023] VGR2922 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2922 gene was

detected is described hereinabove with reference to Figs. 1-9.

[2024] VGR2922 gene encodes VGR2922 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2025] VGR2922 precursor RNA folds spatially, forming VGR2922 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2922 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2922 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2026] VGR2922 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM901 precursor RNA and VGAM902 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM

FOLDED PRECURSOR RNA of Fig. 1.

[2027] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM901 RNA and VGAM902 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2028] VGAM901 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM901 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM901 host target RNA into VGAM901 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2029] VGAM902 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM902 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM902 host target RNA into VGAM902 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2030] It is appreciated that a function of VGR2922 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2922 gene include diagnosis, prevention and treatment of viral infection by Sulfolobus Virus SIRV-1. Specific functions, and accordingly utilities, of VGR2922 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2922 gene: VGAM901 host target protein and VGAM902 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM901 and VGAM902. Fig. 9 further

provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2923(VGR2923) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2031] VGR2923 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2923 gene was detected is described hereinabove with reference to Figs. 1-9.

[2032] VGR2923 gene encodes VGR2923 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2033] VGR2923 precursor RNA folds spatially, forming VGR2923 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2923 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2923 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2034] VGR2923 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM903 precursor RNA and VGAM904 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2035] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM903 RNA and VGAM904 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2036] VGAM903 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM903 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM903 host target RNA into VGAM903 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2037] VGAM904 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM904 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM904 host target RNA into VGAM904 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2038] It is appreciated that a function of VGR2923 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2923 gene include diagnosis, prevention and treatment of viral infection by

Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGR2923 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2923 gene: VGAM903 host target protein and VGAM904 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM903 and VGAM904. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2924(VGR2924) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2039] VGR2924 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2924 gene was detected is described hereinabove with reference to Figs. 1-9.

- [2040] VGR2924 gene encodes VGR2924 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2041] VGR2924 precursor RNA folds spatially, forming VGR2924 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2924 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2924 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2042] VGR2924 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM905 precursor RNA, VGAM906 precursor RNA, VGAM907 precursor RNA and VGAM908 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2043] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM905 RNA, VGAM906 RNA, VGAM907 RNA and VGAM908 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2044] VGAM905 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM905 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM905 host target RNA into VGAM905 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2045] VGAM906 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM906 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM906 host target RNA into VGAM906 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2046] VGAM907 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM907 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM907 host target RNA into VGAM907 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2047] VGAM908 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM908 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM908 host target RNA into VGAM908 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2048] It is appreciated that a function of VGR2924 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2924 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2924 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2924 gene: VGAM905 host target protein, VGAM906 host target protein, VGAM907 host target protein and VGAM908 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The

function of these host target genes is elaborated herein—above with reference to VGAM905, VGAM906, VGAM907 and VGAM908. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2925 (VGR2925) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2049] VGR2925 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2925 gene was detected is described hereinabove with reference to Figs. 1–9.

[2050] VGR2925 gene encodes VGR2925 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2051] VGR2925 precursor RNA folds spatially, forming VGR2925 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2925 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2925 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2052] VGR2925 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM909 precursor RNA and VGAM910 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2053] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM909 RNA and VGAM910 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2054] VGAM909 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM909 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM909 host target RNA into VGAM909 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2055] VGAM910 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM910 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM910 host target RNA into VGAM910 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2056] It is appreciated that a function of VGR2925 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2925 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2925 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2925 gene: VGAM909 host target protein and VGAM910 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM909 and VGAM910. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2926(VGR2926) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2057] VGR2926 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2926 gene was detected is described hereinabove with reference to Figs. 1–9.

[2058] VGR2926 gene encodes VGR2926 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2059] VGR2926 precursor RNA folds spatially, forming VGR2926 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2926 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2926 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[2060] VGR2926 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM911 precursor RNA and VGAM912 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2061] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM911 RNA and VGAM912 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2062] VGAM911 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM911 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM911 host target RNA into VGAM911 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2063] VGAM912 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM912 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM912 host target RNA into VGAM912 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2064] It is appreciated that a function of VGR2926 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2926 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGR2926 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2926 gene: VGAM911 host target protein and VGAM912 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM911 and VGAM912. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2927 (VGR2927) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2065] VGR2927 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2927 gene was detected is described hereinabove with reference to Figs. 1-9.

[2066] VGR2927 gene encodes VGR2927 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2067] VGR2927 precursor RNA folds spatially, forming VGR2927 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2927 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2927 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2068] VGR2927 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM913 precursor RNA and VGAM914 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2069] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM913 RNA and VGAM914 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2070] VGAM913 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM913 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM913 host target RNA into VGAM913 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2071] VGAM914 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM914 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM914 host target RNA into VGAM914 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2072] It is appreciated that a function of VGR2927 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2927 gene include diagnosis, prevention and treatment of viral infection by Pothos Latent Virus. Specific functions, and accordingly utilities, of VGR2927 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2927 gene: VGAM913 host target protein and VGAM914 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM913 and VGAM914. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2928(VGR2928) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2073] VGR2928 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2928 gene was

detected is described hereinabove with reference to Figs. 1-9.

[2074] VGR2928 gene encodes VGR2928 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2075] VGR2928 precursor RNA folds spatially, forming VGR2928 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2928 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2928 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2076] VGR2928 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM915 precursor RNA and VGAM916 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM

FOLDED PRECURSOR RNA of Fig. 1.

[2077] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM915 RNA and VGAM916 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2078] VGAM915 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM915 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM915 host target RNA into VGAM915 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2079] VGAM916 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM916 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM916 host target RNA into VGAM916 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2080] It is appreciated that a function of VGR2928 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2928 gene include diagnosis, prevention and treatment of viral infection by Trichoplusia Ni Cytoplasmic Polyhedrosis Virus 15. Specific functions, and accordingly utilities, of VGR2928 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2928 gene: VGAM915 host target protein and VGAM916 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM915 and

VGAM916.Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2929(VGR2929) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2081] VGR2929 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2929 gene was detected is described hereinabove with reference to Figs. 1-9.

[2082] VGR2929 gene encodes VGR2929 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2083] VGR2929 precursor RNA folds spatially, forming VGR2929 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2929 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2929 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2084] VGR2929 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM918 precursor RNA and VGAM919 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2085] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM918 RNA and VGAM919 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2086] VGAM918 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM918 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM918 host target RNA into VGAM918 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2087] VGAM919 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM919 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM919 host target RNA into VGAM919 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2088] It is appreciated that a function of VGR2929 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2929 gene include

diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGR2929 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2929 gene: VGAM918 host target protein and VGAM919 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM918 and VGAM919. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2930(VGR2930) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2089] VGR2930 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2930 gene was detected is described hereinabove with reference to Figs. 1-9.

- [2090] VGR2930 gene encodes VGR2930 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2091] VGR2930 precursor RNA folds spatially, forming VGR2930 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2930 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2930 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2092] VGR2930 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM921 precursor RNA, VGAM922 precursor RNA and VGAM923 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2093] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM921 RNA, VGAM922 RNA and VGAM923 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2094] VGAM921 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM921 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM921 host target RNA into VGAM921 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2095] VGAM922 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM922 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM922 host target RNA into VGAM922 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2096] VGAM923 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM923 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM923 host target RNA into VGAM923 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2097] It is appreciated that a function of VGR2930 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2930 gene include diagnosis, prevention and treatment of viral infection by Peanut Clump Virus. Specific functions, and accordingly utilities, of VGR2930 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2930 gene: VGAM921 host target protein, VGAM922 host target protein and VGAM923 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM921, VGAM922 and VGAM923. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2931(VGR2931) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2098] VGR2931 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2931 gene was

detected is described hereinabove with reference to Figs. 1-9.

[2099] VGR2931 gene encodes VGR2931 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2100] VGR2931 precursor RNA folds spatially, forming VGR2931 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2931 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2931 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2101] VGR2931 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM924 precursor RNA, VGAM925 precursor RNA, VGAM926 precursor RNA, VGAM927 precursor RNA, VGAM928 precursor RNA and VGAM929 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR,

each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2102] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM924 RNA, VGAM925 RNA, VGAM926 RNA, VGAM927 RNA, VGAM928 RNA and VGAM929 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2103] VGAM924 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM924 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM924 host target RNA into VGAM924 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2104] VGAM925 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM925 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM925 host target RNA into VGAM925 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2105] VGAM926 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM926 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM926 host target RNA into VGAM926 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2106] VGAM927 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM927 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM927 host target RNA into VGAM927 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2107] VGAM928 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM928 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM928 host target RNA into VGAM928 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2108] VGAM929 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM929 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM929 host target RNA into VGAM929 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2109] It is appreciated that a function of VGR2931 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2931 gene include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGR2931 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2931 gene:

VGAM924 host target protein, VGAM925 host target protein, VGAM926 host target protein, VGAM927 host target protein, VGAM928 host target protein and VGAM929 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM924, VGAM925, VGAM926, VGAM927, VGAM928 and VGAM929. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2932(VGR2932) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2110] VGR2932 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2932 gene was detected is described hereinabove with reference to Figs. 1-9.

[2111] VGR2932 gene encodes VGR2932 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2112] VGR2932 precursor RNA folds spatially, forming VGR2932 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2932 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2932 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2113] VGR2932 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM932 precursor RNA, VGAM933 precursor RNA and VGAM934 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2114] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM932 RNA, VGAM933 RNA and VGAM934 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2115] VGAM932 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM932 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM932 host target RNA into VGAM932 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2116] VGAM933 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM933 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM933 host target RNA into VGAM933 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2117] VGAM934 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM934 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM934 host target RNA into VGAM934 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2118] It is appreciated that a function of VGR2932 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2932 gene include diagnosis, prevention and treatment of viral infection by

Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2932 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2932 gene: VGAM932 host target protein, VGAM933 host target protein and VGAM934 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM932, VGAM933 and VGAM934. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2933(VGR2933) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2119] VGR2933 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2933 gene was detected is described hereinabove with reference to Figs. 1-9.

- [2120] VGR2933 gene encodes VGR2933 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2121] VGR2933 precursor RNA folds spatially, forming VGR2933 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2933 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2933 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2122] VGR2933 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM935 precursor RNA, VGAM936 precursor RNA and VGAM937 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2123] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM935 RNA, VGAM936 RNA and VGAM937 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2124] VGAM935 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM935 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM935 host target RNA into VGAM935 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2125] VGAM936 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM936 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM936 host target RNA into VGAM936 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2126] VGAM937 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM937 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM937 host target RNA into VGAM937 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2127] It is appreciated that a function of VGR2933 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR2933 gene include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGR2933 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2933 gene: VGAM935 host target protein, VGAM936 host target protein and VGAM937 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM935, VGAM936 and VGAM937. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2934(VGR2934) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2128] VGR2934 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2934 gene was detected is described hereinabove with reference to Figs. 1–9.

[2129] VGR2934 gene encodes VGR2934 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2130] VGR2934 precursor RNA folds spatially, forming VGR2934 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2934 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2934 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[2131] VGR2934 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM938 precursor RNA, VGAM939 precursor RNA and VGAM940 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2132] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM938 RNA, VGAM939 RNA and VGAM940 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2133] VGAM938 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM938 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM938 host target RNA into VGAM938 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2134] VGAM939 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM939 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM939 host target RNA into VGAM939 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2135] VGAM940 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM940 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM940 host target RNA into VGAM940 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2136] It is appreciated that a function of VGR2934 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2934 gene include diagnosis, prevention and treatment of viral infection by Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGR2934 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2934 gene: VGAM938 host target protein, VGAM939 host target protein and VGAM940 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM938, VGAM939 and VGAM940. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2935(VGR2935) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2137] VGR2935 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2935 gene was detected is described hereinabove with reference to Figs. 1-9.

[2138] VGR2935 gene encodes VGR2935 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2139] VGR2935 precursor RNA folds spatially, forming VGR2935 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2935 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2935 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2140] VGR2935 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM941 precursor RNA, VGAM942 precursor RNA and VGAM943 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2141] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM941 RNA, VGAM942 RNA and VGAM943 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2142] VGAM941 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM941 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM941 host target RNA into VGAM941 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2143] VGAM942 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM942 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM942 host target RNA into VGAM942 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2144] VGAM943 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM943 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM943 host target RNA into VGAM943 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2145] It is appreciated that a function of VGR2935 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2935 gene include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGR2935 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2935 gene: VGAM941 host target protein, VGAM942 host target protein and VGAM943 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM941, VGAM942 and VGAM943. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2936(VGR2936) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates ex-

pression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2146] VGR2936 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2936 gene was detected is described hereinabove with reference to Figs. 1-9.

[2147] VGR2936 gene encodes VGR2936 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2148] VGR2936 precursor RNA folds spatially, forming VGR2936 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2936 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2936 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2149] VGR2936 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM944 precursor RNA and VGAM945 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2150] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM944 RNA and VGAM945 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2151] VGAM944 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM944 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM944 host target RNA into VGAM944 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2152] VGAM945 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM945 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM945 host target RNA into VGAM945 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2153] It is appreciated that a function of VGR2936 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2936 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2936 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2936 gene: VGAM944 host target protein and VGAM945 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM944 and VGAM945. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2937(VGR2937) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2154] VGR2937 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2937 gene was detected is described hereinabove with reference to Figs. 1-9.

[2155] VGR2937 gene encodes VGR2937 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2156] VGR2937 precursor RNA folds spatially, forming VGR2937 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2937 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2937 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2157] VGR2937 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM946 precursor RNA and VGAM947 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2158] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM946 RNA and VGAM947 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2159] VGAM946 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM946 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM946 host target RNA into VGAM946 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2160] VGAM947 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM947 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM947 host target RNA into VGAM947 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2161] It is appreciated that a function of VGR2937 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2937 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGR2937 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2937 gene: VGAM946 host target protein and VGAM947 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM946 and VGAM947. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2938(VGR2938) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2162] VGR2938 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2938 gene was detected is described hereinabove with reference to Figs. 1–9.

[2163] VGR2938 gene encodes VGR2938 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2164] VGR2938 precursor RNA folds spatially, forming VGR2938 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2938 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2938 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[2165] VGR2938 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM948 precursor RNA and VGAM949 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2166] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM948 RNA and VGAM949 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2167] VGAM948 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM948 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM948 host target RNA into VGAM948 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2168] VGAM949 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM949 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM949 host target RNA into VGAM949 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2169] It is appreciated that a function of VGR2938 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2938 gene include diagnosis, prevention and treatment of viral infection by Carnation Italian Ringspot Virus. Specific functions, and accordingly utilities, of VGR2938 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2938 gene: VGAM948 host target protein and VGAM949 host target protein, herein schematically represented by VGAM1 HOST TARGET

PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM948 and VGAM949. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2939(VGR2939) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2170] VGR2939 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2939 gene was detected is described hereinabove with reference to Figs. 1–9.

[2171] VGR2939 gene encodes VGR2939 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2172] VGR2939 precursor RNA folds spatially, forming VGR2939 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2939 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2939 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2173] VGR2939 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM950 precursor RNA, VGAM951 precursor RNA and VGAM952 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2174] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM950 RNA, VGAM951 RNA and VGAM952 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2175] VGAM950 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM950 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM950 host target RNA into VGAM950 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2176] VGAM951 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM951 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM951 host target RNA into VGAM951 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2177] VGAM952 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM952 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM952 host target RNA into VGAM952 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2178] It is appreciated that a function of VGR2939 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2939 gene include diagnosis, prevention and treatment of viral infection by Tomato Bushy Stunt Virus. Specific functions, and accordingly utilities, of VGR2939 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2939 gene: VGAM950 host

target protein, VGAM951 host target protein and VGAM952 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM950, VGAM951 and VGAM952. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2940 (VGR2940) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2179] VGR2940 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2940 gene was detected is described hereinabove with reference to Figs. 1-9.

[2180] VGR2940 gene encodes VGR2940 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2181] VGR2940 precursor RNA folds spatially, forming VGR2940 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2940 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2940 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2182] VGR2940 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM953 precursor RNA, VGAM954 precursor RNA, VGAM955 precursor RNA, VGAM956 precursor RNA, VGAM957 precursor RNA and VGAM958 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2183] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM953 RNA, VGAM954 RNA, VGAM955 RNA, VGAM956 RNA,

VGAM957 RNA and VGAM958 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2184] VGAM953 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM953 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM953 host target RNA into VGAM953 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2185] VGAM954 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM954 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM954 host target RNA into VGAM954 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2186] VGAM955 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM955 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM955 host target RNA into VGAM955 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2187] VGAM956 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM956 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM956 host target RNA into VGAM956 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2188] VGAM957 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM957 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM957 host target RNA into VGAM957 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2189] VGAM958 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM958 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM958 host target RNA into VGAM958 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2190] It is appreciated that a function of VGR2940 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2940 gene include diagnosis, prevention and treatment of viral infection by Tomato Spotted Wilt Virus. Specific functions, and accordingly utilities, of VGR2940 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2940 gene: VGAM953 host target protein, VGAM954 host target protein, VGAM955 host target protein, VGAM956 host target protein, VGAM957 host target protein and VGAM958 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM953, VGAM954,

VGAM955, VGAM956, VGAM957 and VGAM958. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2941 (VGR2941) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2191] VGR2941 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2941 gene was detected is described hereinabove with reference to Figs. 1-9.

[2192] VGR2941 gene encodes VGR2941 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2193] VGR2941 precursor RNA folds spatially, forming VGR2941 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2941 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2941 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2194] VGR2941 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM959 precursor RNA, VGAM960 precursor RNA and VGAM961 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2195] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM959 RNA, VGAM960 RNA and VGAM961 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2196] VGAM959 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM959 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM959 host target RNA into VGAM959 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2197] VGAM960 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM960 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM960 host target RNA into VGAM960 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2198] VGAM961 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM961 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM961 host target RNA into VGAM961 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2199] It is appreciated that a function of VGR2941 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2941 gene include diagnosis, prevention and treatment of viral infection by Lumpy Skin Disease Virus. Specific functions, and accordingly utilities, of VGR2941 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2941 gene: VGAM959 host target protein, VGAM960 host target protein and VGAM961 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM959, VGAM960 and VGAM961. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2942 (VGR2942) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2200] VGR2942 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2942 gene was detected is described hereinabove with reference to Figs. 1-9.

[2201] VGR2942 gene encodes VGR2942 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2202] VGR2942 precursor RNA folds spatially, forming VGR2942 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2942 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2942 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2203] VGR2942 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM962 precursor RNA, VGAM963 precursor RNA, VGAM964 precursor RNA, VGAM965 precursor RNA and VGAM966 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2204] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM962 RNA, VGAM963 RNA, VGAM964 RNA, VGAM965 RNA and VGAM966 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2205] VGAM962 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM962 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM962 host target RNA into VGAM962 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2206] VGAM963 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM963 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM963 host target RNA into VGAM963 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN, all of Fig. 1.

[2207] VGAM964 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM964 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM964 host target RNA into VGAM964 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2208] VGAM965 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM965 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM965 host target RNA into VGAM965 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2209] VGAM966 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM966 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM966 host target RNA into VGAM966 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2210] It is appreciated that a function of VGR2942 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2942 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2942 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2942 gene: VGAM962 host target protein, VGAM963 host target protein, VGAM964 host target protein, VGAM965 host target protein and VGAM966 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM962, VGAM963, VGAM964, VGAM965 and VGAM966. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2943(VGR2943) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2211] VGR2943 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2943 gene was detected is described hereinabove with reference to Figs. 1-9.

[2212] VGR2943 gene encodes VGR2943 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2213] VGR2943 precursor RNA folds spatially, forming VGR2943 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2943 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2943 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2214] VGR2943 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM967 precursor RNA, VGAM968 precursor RNA, VGAM969 precursor RNA and VGAM970 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2215] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM967 RNA, VGAM968 RNA, VGAM969 RNA and VGAM970 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2216] VGAM967 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM967 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM967 host target RNA into VGAM967 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2217] VGAM968 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM968 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM968 host target RNA into VGAM968 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2218] VGAM969 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM969 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM969 host target RNA into VGAM969 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2219] VGAM970 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM970 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM970 host target RNA into VGAM970 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2220] It is appreciated that a function of VGR2943 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2943 gene include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGR2943 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2943 gene: VGAM967 host target protein, VGAM968 host target protein, VGAM969 host target protein and VGAM970 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM967, VGAM968, VGAM969

and VGAM970. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2944 (VGR2944) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2221] VGR2944 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2944 gene was detected is described hereinabove with reference to Figs. 1-9.

[2222] VGR2944 gene encodes VGR2944 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2223] VGR2944 precursor RNA folds spatially, forming VGR2944 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2944 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2944 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2224] VGR2944 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM971 precursor RNA and VGAM972 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2225] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM971 RNA and VGAM972 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2226] VGAM971 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM971 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM971 host target RNA into VGAM971 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2227] VGAM972 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM972 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM972 host target RNA into VGAM972 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2228] It is appreciated that a function of VGR2944 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2944 gene include

diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGR2944 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2944 gene: VGAM971 host target protein and VGAM972 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM971 and VGAM972. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2945(VGR2945) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2229] VGR2945 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2945 gene was detected is described hereinabove with reference to Figs.

1-9.

- [2230] VGR2945 gene encodes VGR2945 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2231] VGR2945 precursor RNA folds spatially, forming VGR2945 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2945 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2945 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2232] VGR2945 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM975 precursor RNA, VGAM976 precursor RNA, VGAM977 precursor RNA, VGAM978 precursor RNA and VGAM979 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corre-

sponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2233] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM975 RNA, VGAM976 RNA, VGAM977 RNA, VGAM978 RNA and VGAM979 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2234] VGAM975 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM975 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM975 host target RNA into VGAM975 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2235] VGAM976 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM976 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM976 host target RNA into VGAM976 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2236] VGAM977 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM977 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM977 host target RNA into VGAM977 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2237] VGAM978 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM978 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM978 host target RNA into VGAM978 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2238] VGAM979 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM979 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM979 host target RNA into VGAM979 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2239] It is appreciated that a function of VGR2945 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2945 gene include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR2945 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2945 gene: VGAM975 host target protein, VGAM976 host target protein, VGAM977 host target protein, VGAM978 host target protein and VGAM979 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM975, VGAM976, VGAM977, VGAM978 and VGAM979. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2946(VGR2946) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in

the art.

- [2240] VGR2946 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2946 gene was detected is described hereinabove with reference to Figs. 1–9.
- [2241] VGR2946 gene encodes VGR2946 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2242] VGR2946 precursor RNA folds spatially, forming VGR2946 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2946 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2946 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.
- [2243] VGR2946 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM980 precursor RNA, VGAM981 pre–

cursor RNA, VGAM982 precursor RNA, VGAM983 precursor RNA and VGAM984 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2244] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM980 RNA, VGAM981 RNA, VGAM982 RNA, VGAM983 RNA and VGAM984 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2245] VGAM980 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM980 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM980 host target RNA into VGAM980 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2246] VGAM981 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM981 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM981 host target RNA into VGAM981 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2247] VGAM982 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM982 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM982 host target RNA into

VGAM982 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2248] VGAM983 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM983 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM983 host target RNA into VGAM983 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2249] VGAM984 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM984 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM984 host target RNA into VGAM984 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2250] It is appreciated that a function of VGR2946 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2946 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR2946 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2946 gene: VGAM980 host target protein, VGAM981 host target protein, VGAM982 host target protein, VGAM983 host target protein and VGAM984 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM980, VGAM981, VGAM982, VGAM983 and VGAM984. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene,

referred to here as Viral Genomic Record 2947(VGR2947) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2251] VGR2947 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2947 gene was detected is described hereinabove with reference to Figs. 1-9.

[2252] VGR2947 gene encodes VGR2947 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2253] VGR2947 precursor RNA folds spatially, forming VGR2947 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2947 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2947 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[2254] VGR2947 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM986 precursor RNA, VGAM987 precursor RNA, VGAM988 precursor RNA, VGAM989 precursor RNA and VGAM990 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2255] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM986 RNA, VGAM987 RNA, VGAM988 RNA, VGAM989 RNA and VGAM990 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2256] VGAM986 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM986 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM986 host target RNA into VGAM986 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2257] VGAM987 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM987 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM987 host target RNA into VGAM987 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2258] VGAM988 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM988 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM988 host target RNA into VGAM988 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2259] VGAM989 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM989 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM989 host target RNA into VGAM989 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2260] VGAM990 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM990 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM990 host target RNA into VGAM990 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2261] It is appreciated that a function of VGR2947 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2947 gene include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-4. Specific functions, and accordingly utilities, of VGR2947 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2947 gene: VGAM986 host target protein, VGAM987 host target protein, VGAM988 host target protein, VGAM989 host target protein and VGAM990 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3

HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM986, VGAM987, VGAM988, VGAM989 and VGAM990. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2948(VGR2948) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2262] VGR2948 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2948 gene was detected is described hereinabove with reference to Figs. 1-9.

[2263] VGR2948 gene encodes VGR2948 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2264] VGR2948 precursor RNA folds spatially, forming VGR2948 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2948 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2948 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2265] VGR2948 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM991 precursor RNA, VGAM992 precursor RNA, VGAM993 precursor RNA, VGAM994 precursor RNA, VGAM995 precursor RNA and VGAM996 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2266] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM991 RNA, VGAM992 RNA, VGAM993 RNA, VGAM994 RNA, VGAM995 RNA and VGAM996 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2267] VGAM991 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM991 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM991 host target RNA into VGAM991 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2268] VGAM992 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM992 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM992 host target RNA into VGAM992 host target protein, herein schematically repre-

sented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2269] VGAM993 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM993 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM993 host target RNA into VGAM993 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2270] VGAM994 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM994 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM994 host target RNA into

VGAM994 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2271] VGAM995 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM995 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM995 host target RNA into VGAM995 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2272] VGAM996 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM996 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM996 host target RNA into VGAM996 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2273] It is appreciated that a function of VGR2948 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2948 gene include diagnosis, prevention and treatment of viral infection by Leishmania RNA Virus 1-1. Specific functions, and accordingly utilities, of VGR2948 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2948 gene: VGAM991 host target protein, VGAM992 host target protein, VGAM993 host target protein, VGAM994 host target protein, VGAM995 host target protein and VGAM996 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM991, VGAM992, VGAM993, VGAM994, VGAM995 and VGAM996. Fig. 9 further provides a conceptual description of novel bioinfor-

matically detected regulatory viral gene, referred to here as Viral Genomic Record 2949(VGR2949) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2274] VGR2949 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2949 gene was detected is described hereinabove with reference to Figs. 1-9.

[2275] VGR2949 gene encodes VGR2949 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2276] VGR2949 precursor RNA folds spatially, forming VGR2949 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2949 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2949 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2277] VGR2949 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM997 precursor RNA, VGAM998 precursor RNA, VGAM999 precursor RNA, VGAM1000 precursor RNA and VGAM1001 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2278] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM997 RNA, VGAM998 RNA, VGAM999 RNA, VGAM1000 RNA and VGAM1001 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2279] VGAM997 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM997 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM997 host target RNA into VGAM997 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2280] VGAM998 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM998 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM998 host target RNA into VGAM998 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2281] VGAM999 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM999 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM999 host target RNA into VGAM999 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2282] VGAM1000 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1000 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1000 host target RNA into VGAM1000 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2283] VGAM1001 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1001 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1001 host target RNA into VGAM1001 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2284] It is appreciated that a function of VGR2949 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2949 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR2949 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2949 gene: VGAM997 host target protein, VGAM998 host target protein, VGAM999 host target protein, VGAM1000 host target protein and VGAM1001 host target protein, herein schematically represented by

VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM997, VGAM998, VGAM999, VGAM1000 and VGAM1001. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2950(VGR2950) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2285] VGR2950 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2950 gene was detected is described hereinabove with reference to Figs. 1-9.

[2286] VGR2950 gene encodes VGR2950 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2287] VGR2950 precursor RNA folds spatially, forming VGR2950 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2950 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2950 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2288] VGR2950 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1002 precursor RNA, VGAM1003 precursor RNA, VGAM1004 precursor RNA, VGAM1005 precursor RNA, VGAM1006 precursor RNA, VGAM1007 precursor RNA and VGAM1008 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2289] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1002 RNA, VGAM1003 RNA, VGAM1004 RNA, VGAM1005 RNA,

VGAM1006 RNA, VGAM1007 RNA and VGAM1008 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2290] VGAM1002 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1002 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1002 host target RNA into VGAM1002 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2291] VGAM1003 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1003 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1003 host target RNA into VGAM1003 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2292] VGAM1004 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1004 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1004 host target RNA into VGAM1004 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2293] VGAM1005 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1005 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1005 host target RNA into VGAM1005 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2294] VGAM1006 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1006 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1006 host target RNA into VGAM1006 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2295] VGAM1007 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1007 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1007 host target RNA into VGAM1007 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2296] VGAM1008 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1008 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1008 host target RNA into VGAM1008 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2297] It is appreciated that a function of VGR2950 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2950 gene include

diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR2950 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2950 gene: VGAM1002 host target protein, VGAM1003 host target protein, VGAM1004 host target protein, VGAM1005 host target protein, VGAM1006 host target protein, VGAM1007 host target protein and VGAM1008 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1002, VGAM1003, VGAM1004, VGAM1005, VGAM1006, VGAM1007 and VGAM1008. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2951(VGR2951) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2298] VGR2951 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2951 gene was detected is described hereinabove with reference to Figs. 1-9.

[2299] VGR2951 gene encodes VGR2951 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2300] VGR2951 precursor RNA folds spatially, forming VGR2951 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2951 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2951 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2301] VGR2951 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1009 precursor RNA, VGAM1010 precursor RNA and VGAM1011 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2302] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1009 RNA, VGAM1010 RNA and VGAM1011 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2303] VGAM1009 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1009 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1009 host target RNA into VGAM1009 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2304] VGAM1010 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1010 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1010 host target RNA into VGAM1010 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2305] VGAM1011 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1011 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1011 host target RNA into VGAM1011 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2306] It is appreciated that a function of VGR2951 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2951 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2951 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2951 gene: VGAM1009 host target protein, VGAM1010 host target protein and VGAM1011 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1009, VGAM1010 and VGAM1011. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2952(VGR2952) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates ex-

pression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2307] VGR2952 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2952 gene was detected is described hereinabove with reference to Figs. 1-9.

[2308] VGR2952 gene encodes VGR2952 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2309] VGR2952 precursor RNA folds spatially, forming VGR2952 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2952 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2952 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2310] VGR2952 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1012 precursor RNA and VGAM1013 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2311] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1012 RNA and VGAM1013 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2312] VGAM1012 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1012 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1012 host target RNA into VGAM1012 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2313] VGAM1013 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1013 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1013 host target RNA into VGAM1013 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2314] It is appreciated that a function of VGR2952 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2952 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2952 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2952 gene: VGAM1012 host target protein and VGAM1013 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1012 and VGAM1013. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2953(VGR2953) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2315] VGR2953 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2953 gene was detected is described hereinabove with reference to Figs. 1-9.

[2316] VGR2953 gene encodes VGR2953 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2317] VGR2953 precursor RNA folds spatially, forming VGR2953

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2953 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2953 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2318] VGR2953 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1015 precursor RNA and VGAM1016 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2319] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1015 RNA and VGAM1016 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2320] VGAM1015 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1015 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1015 host target RNA into VGAM1015 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2321] VGAM1016 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1016 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1016 host target RNA into VGAM1016 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2322] It is appreciated that a function of VGR2953 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2953 gene include diagnosis, prevention and treatment of viral infection by Broad Bean Necrosis Virus. Specific functions, and accordingly utilities, of VGR2953 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2953 gene: VGAM1015 host target protein and VGAM1016 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1015 and VGAM1016. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2954(VGR2954) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[2323] VGR2954 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2954 gene was detected is described hereinabove with reference to Figs. 1-9.

[2324] VGR2954 gene encodes VGR2954 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2325] VGR2954 precursor RNA folds spatially, forming VGR2954 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2954 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2954 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2326] VGR2954 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM1017 precursor RNA, VGAM1018 precursor RNA and VGAM1019 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2327] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1017 RNA, VGAM1018 RNA and VGAM1019 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2328] VGAM1017 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1017 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1017 host target RNA into

VGAM1017 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2329] VGAM1018 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1018 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1018 host target RNA into VGAM1018 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2330] VGAM1019 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1019 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1019 host target RNA into VGAM1019 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2331] It is appreciated that a function of VGR2954 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2954 gene include diagnosis, prevention and treatment of viral infection by Beet Western Yellows Virus. Specific functions, and accordingly utilities, of VGR2954 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2954 gene: VGAM1017 host target protein, VGAM1018 host target protein and VGAM1019 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1017, VGAM1018 and VGAM1019. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2955(VGR2955) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2332] VGR2955 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2955 gene was detected is described hereinabove with reference to Figs. 1-9.

[2333] VGR2955 gene encodes VGR2955 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2334] VGR2955 precursor RNA folds spatially, forming VGR2955 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2955 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2955 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

- [2335] VGR2955 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1020 precursor RNA, VGAM1021 precursor RNA, VGAM1022 precursor RNA, VGAM1023 precursor RNA, VGAM1024 precursor RNA, VGAM1025 precursor RNA and VGAM1026 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.
- [2336] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1020 RNA, VGAM1021 RNA, VGAM1022 RNA, VGAM1023 RNA, VGAM1024 RNA, VGAM1025 RNA and VGAM1026 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2337] VGAM1020 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1020 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1020 host target RNA into VGAM1020 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2338] VGAM1021 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1021 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1021 host target RNA into VGAM1021 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2339] VGAM1022 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1022 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1022 host target RNA into VGAM1022 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2340] VGAM1023 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1023 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1023 host target RNA into VGAM1023 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2341] VGAM1024 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1024 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1024 host target RNA into VGAM1024 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2342] VGAM1025 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1025 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1025 host target RNA into VGAM1025 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2343] VGAM1026 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1026 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1026 host target RNA into VGAM1026 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2344] It is appreciated that a function of VGR2955 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2955 gene include diagnosis, prevention and treatment of viral infection by Cereal Yellow Dwarf Virus – RPV. Specific functions, and accordingly utilities, of VGR2955 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2955 gene: VGAM1020 host target protein, VGAM1021 host target protein,

VGAM1022 host target protein, VGAM1023 host target protein, VGAM1024 host target protein, VGAM1025 host target protein and VGAM1026 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1020, VGAM1021, VGAM1022, VGAM1023, VGAM1024, VGAM1025 and VGAM1026. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2956(VGR2956) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2345] VGR2956 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2956 gene was detected is described hereinabove with reference to Figs. 1-9.

[2346] VGR2956 gene encodes VGR2956 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2347] VGR2956 precursor RNA folds spatially, forming VGR2956 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2956 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2956 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2348] VGR2956 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1027 precursor RNA and VGAM1028 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2349] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1027

RNA and VGAM1028 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2350] VGAM1027 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1027 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1027 host target RNA into VGAM1027 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2351] VGAM1028 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1028 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1028 host target RNA into VGAM1028 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2352] It is appreciated that a function of VGR2956 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2956 gene include diagnosis, prevention and treatment of viral infection by Ictalurid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2956 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2956 gene: VGAM1027 host target protein and VGAM1028 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1027 and VGAM1028. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2957(VGR2957) viral gene, which encodes an `operon-like` cluster of novel viral micro

RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2353] VGR2957 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2957 gene was detected is described hereinabove with reference to Figs. 1-9.

[2354] VGR2957 gene encodes VGR2957 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2355] VGR2957 precursor RNA folds spatially, forming VGR2957 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2957 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2957 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2356] VGR2957 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1030 precursor RNA and VGAM1031 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2357] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1030 RNA and VGAM1031 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2358] VGAM1030 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1030 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1030 host target RNA into

VGAM1030 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2359] VGAM1031 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1031 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1031 host target RNA into VGAM1031 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2360] It is appreciated that a function of VGR2957 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2957 gene include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGR2957 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2957 gene: VGAM1030 host target protein and VGAM1031 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1030 and VGAM1031. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2958(VGR2958) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

- [2361] VGR2958 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2958 gene was detected is described hereinabove with reference to Figs. 1-9.
- [2362] VGR2958 gene encodes VGR2958 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2363] VGR2958 precursor RNA folds spatially, forming VGR2958 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2958 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2958 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2364] VGR2958 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1032 precursor RNA, VGAM1033 precursor RNA, VGAM1034 precursor RNA, VGAM1035 precursor RNA and VGAM1036 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2365] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1032 RNA, VGAM1033 RNA, VGAM1034 RNA, VGAM1035 RNA and VGAM1036 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2366] VGAM1032 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1032 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1032 host target RNA into VGAM1032 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2367] VGAM1033 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1033 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1033 host target RNA into VGAM1033 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2368] VGAM1034 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1034 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1034 host target RNA into VGAM1034 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2369] VGAM1035 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1035 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1035 host target RNA into VGAM1035 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2370] VGAM1036 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1036 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1036 host target RNA into VGAM1036 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2371] It is appreciated that a function of VGR2958 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2958 gene include

diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2958 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2958 gene: VGAM1032 host target protein, VGAM1033 host target protein, VGAM1034 host target protein, VGAM1035 host target protein and VGAM1036 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1032, VGAM1033, VGAM1034, VGAM1035 and VGAM1036. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2959(VGR2959) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2372] VGR2959 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR2959 gene was detected is described hereinabove with reference to Figs. 1–9.

[2373] VGR2959 gene encodes VGR2959 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2374] VGR2959 precursor RNA folds spatially, forming VGR2959 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2959 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2959 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[2375] VGR2959 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1037 precursor RNA, VGAM1038 precursor RNA, VGAM1039 precursor RNA and VGAM1040 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2376] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1037 RNA, VGAM1038 RNA, VGAM1039 RNA and VGAM1040 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2377] VGAM1037 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1037 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1037 host target RNA into VGAM1037 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2378] VGAM1038 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1038 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1038 host target RNA into VGAM1038 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2379] VGAM1039 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1039 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1039 host target RNA into VGAM1039 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2380] VGAM1040 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1040 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1040 host target RNA into VGAM1040 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2381] It is appreciated that a function of VGR2959 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2959 gene include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGR2959 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2959 gene: VGAM1037 host target protein, VGAM1038 host target protein,

VGAM1039 host target protein and VGAM1040 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1037, VGAM1038, VGAM1039 and VGAM1040. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2960 (VGR2960) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2382] VGR2960 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2960 gene was detected is described hereinabove with reference to Figs. 1-9.

[2383] VGR2960 gene encodes VGR2960 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2384] VGR2960 precursor RNA folds spatially, forming VGR2960 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2960 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2960 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2385] VGR2960 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1041 precursor RNA, VGAM1042 precursor RNA and VGAM1043 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2386] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1041 RNA, VGAM1042 RNA and VGAM1043 RNA, herein schematically represented by VGAM1 RNA through VGAM3

RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2387] VGAM1041 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1041 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1041 host target RNA into VGAM1041 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2388] VGAM1042 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1042 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1042 host target RNA into

VGAM1042 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2389] VGAM1043 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1043 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1043 host target RNA into VGAM1043 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2390] It is appreciated that a function of VGR2960 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2960 gene include diagnosis, prevention and treatment of viral infection by White Clover Mosaic Virus. Specific functions, and accordingly utilities, of VGR2960 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2960 gene: VGAM1041 host
target protein, VGAM1042 host target protein and
VGAM1043 host target protein, herein schematically rep-
resented by VGAM1 HOST TARGET PROTEIN through
VGAM3 HOST TARGET PROTEIN. The function of these
host target genes is elaborated hereinabove with refer-
ence to VGAM1041, VGAM1042 and VGAM1043. Fig. 9
further provides a conceptual description of novel bioin-
formatically detected regulatory viral gene, referred to
here as Viral Genomic Record 2961(VGR2961) viral gene,
which encodes an `operon-like` cluster of novel viral mi-
cro RNA-like genes, each of which in turn modulates ex-
pression of at least one host target gene, the function and
utility of which at least one host target gene is known in
the art.

[2391] VGR2961 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2961 gene was
detected is described hereinabove with reference to Figs.
1-9.

[2392] VGR2961 gene encodes VGR2961 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2393] VGR2961 precursor RNA folds spatially, forming VGR2961 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2961 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2961 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2394] VGR2961 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1044 precursor RNA, VGAM1045 precursor RNA and VGAM1046 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2395] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1044 RNA, VGAM1045 RNA and VGAM1046 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2396] VGAM1044 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1044 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1044 host target RNA into VGAM1044 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2397] VGAM1045 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1045 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1045 host target RNA into VGAM1045 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2398] VGAM1046 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1046 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1046 host target RNA into VGAM1046 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2399] It is appreciated that a function of VGR2961 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2961 gene include diagnosis, prevention and treatment of viral infection by

Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGR2961 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2961 gene: VGAM1044 host target protein, VGAM1045 host target protein and VGAM1046 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1044, VGAM1045 and VGAM1046. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2962(VGR2962) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2400] VGR2962 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2962 gene was detected is described hereinabove with reference to Figs.

1-9.

[2401] VGR2962 gene encodes VGR2962 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2402] VGR2962 precursor RNA folds spatially, forming VGR2962 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2962 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2962 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2403] VGR2962 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1047 precursor RNA, VGAM1048 precursor RNA and VGAM1049 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[2404] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1047 RNA, VGAM1048 RNA and VGAM1049 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2405] VGAM1047 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1047 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1047 host target RNA into VGAM1047 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2406] VGAM1048 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1048 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1048 host target RNA into VGAM1048 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2407] VGAM1049 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1049 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1049 host target RNA into VGAM1049 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2408] It is appreciated that a function of VGR2962 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2962 gene include diagnosis, prevention and treatment of viral infection by Strawberry Mild Yellow Edge Virus. Specific functions, and accordingly utilities, of VGR2962 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2962 gene: VGAM1047 host target protein, VGAM1048 host target protein and VGAM1049 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1047, VGAM1048 and VGAM1049. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2963(VGR2963) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2409] VGR2963 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2963 gene was detected is described hereinabove with reference to Figs. 1-9.

[2410] VGR2963 gene encodes VGR2963 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2411] VGR2963 precursor RNA folds spatially, forming VGR2963 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2963 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2963 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2412] VGR2963 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1050 precursor RNA, VGAM1051 precursor RNA, VGAM1052 precursor RNA and VGAM1053 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2413] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1050 RNA, VGAM1051 RNA, VGAM1052 RNA and VGAM1053 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2414] VGAM1050 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1050 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1050 host target RNA into VGAM1050 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2415] VGAM1051 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1051 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1051 host target RNA into VGAM1051 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2416] VGAM1052 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1052 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1052 host target RNA into VGAM1052 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2417] VGAM1053 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1053 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1053 host target RNA into VGAM1053 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2418] It is appreciated that a function of VGR2963 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2963 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2963 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2963 gene: VGAM1050 host

target protein, VGAM1051 host target protein, VGAM1052 host target protein and VGAM1053 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM1050, VGAM1051, VGAM1052 and VGAM1053. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2964(VGR2964) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2419] VGR2964 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2964 gene was detected is described hereinabove with reference to Figs. 1–9.

[2420] VGR2964 gene encodes VGR2964 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2421] VGR2964 precursor RNA folds spatially, forming VGR2964

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2964 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2964 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2422] VGR2964 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1055 precursor RNA and VGAM1056 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2423] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1055 RNA and VGAM1056 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2424] VGAM1055 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1055 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1055 host target RNA into VGAM1055 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2425] VGAM1056 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1056 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1056 host target RNA into VGAM1056 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2426] It is appreciated that a function of VGR2964 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2964 gene include diagnosis, prevention and treatment of viral infection by Mayaro Virus. Specific functions, and accordingly utilities, of VGR2964 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2964 gene: VGAM1055 host target protein and VGAM1056 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1055 and VGAM1056. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2965(VGR2965) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of

which at least one host target gene is known in the art.

[2427] VGR2965 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2965 gene was detected is described hereinabove with reference to Figs. 1-9.

[2428] VGR2965 gene encodes VGR2965 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2429] VGR2965 precursor RNA folds spatially, forming VGR2965 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2965 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2965 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2430] VGR2965 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1057 precursor RNA, VGAM1058

precursor RNA and VGAM1059 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2431] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1057 RNA, VGAM1058 RNA and VGAM1059 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2432] VGAM1057 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1057 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1057 host target RNA into VGAM1057 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2433] VGAM1058 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1058 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1058 host target RNA into VGAM1058 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2434] VGAM1059 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1059 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1059 host target RNA into

VGAM1059 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2435] It is appreciated that a function of VGR2965 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2965 gene include diagnosis, prevention and treatment of viral infection by Murid Herpesvirus 4. Specific functions, and accordingly utilities, of VGR2965 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2965 gene: VGAM1057 host target protein, VGAM1058 host target protein and VGAM1059 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1057, VGAM1058 and VGAM1059. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2966(VGR2966) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2436] VGR2966 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2966 gene was detected is described hereinabove with reference to Figs. 1-9.

[2437] VGR2966 gene encodes VGR2966 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2438] VGR2966 precursor RNA folds spatially, forming VGR2966 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2966 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2966 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2439] VGR2966 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1061 precursor RNA and VGAM1062 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2440] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1061 RNA and VGAM1062 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2441] VGAM1061 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1061 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1061 host target RNA into

VGAM1061 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2442] VGAM1062 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1062 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1062 host target RNA into VGAM1062 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2443] It is appreciated that a function of VGR2966 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2966 gene include diagnosis, prevention and treatment of viral infection by Canine Adenovirus Type 1. Specific functions, and accordingly utilities, of VGR2966 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR2966 gene: VGAM1061 host
target protein and VGAM1062 host target protein, herein
schematically represented by VGAM1 HOST TARGET PRO-
TEIN through VGAM3 HOST TARGET PROTEIN. The func-
tion of these host target genes is elaborated hereinabove
with reference to VGAM1061 and VGAM1062. Fig. 9 fur-
ther provides a conceptual description of novel bioinfor-
matically detected regulatory viral gene, referred to here
as Viral Genomic Record 2967(VGR2967) viral gene, which
encodes an `operon-like` cluster of novel viral micro
RNA-like genes, each of which in turn modulates expres-
sion of at least one host target gene, the function and
utility of which at least one host target gene is known in
the art.

[2444] VGR2967 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR2967 gene was
detected is described hereinabove with reference to Figs.
1-9.

[2445] VGR2967 gene encodes VGR2967 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[2446] VGR2967 precursor RNA folds spatially, forming VGR2967 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2967 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2967 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2447] VGR2967 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1063 precursor RNA, VGAM1064 precursor RNA, VGAM1065 precursor RNA and VGAM1066 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2448] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1063

RNA, VGAM1064 RNA, VGAM1065 RNA and VGAM1066 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2449] VGAM1063 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1063 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1063 host target RNA into VGAM1063 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2450] VGAM1064 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1064 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1064 host target RNA into VGAM1064 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2451] VGAM1065 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1065 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1065 host target RNA into VGAM1065 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2452] VGAM1066 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1066 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1066 host target RNA into VGAM1066 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2453] It is appreciated that a function of VGR2967 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2967 gene include diagnosis, prevention and treatment of viral infection by Tulip Virus X. Specific functions, and accordingly utilities, of VGR2967 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2967 gene: VGAM1063 host target protein, VGAM1064 host target protein, VGAM1065 host target protein and VGAM1066 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1063, VGAM1064, VGAM1065 and VGAM1066. Fig. 9 further provides a conceptual descrip-

tion of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2968(VGR2968) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2454] VGR2968 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2968 gene was detected is described hereinabove with reference to Figs. 1-9.

[2455] VGR2968 gene encodes VGR2968 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2456] VGR2968 precursor RNA folds spatially, forming VGR2968 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2968 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2968 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2457] VGR2968 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1067 precursor RNA, VGAM1068 precursor RNA, VGAM1069 precursor RNA, VGAM1070 precursor RNA, VGAM1071 precursor RNA, VGAM1072 precursor RNA, VGAM1073 precursor RNA and VGAM1074 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2458] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1067 RNA, VGAM1068 RNA, VGAM1069 RNA, VGAM1070 RNA, VGAM1071 RNA, VGAM1072 RNA, VGAM1073 RNA and VGAM1074 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2459] VGAM1067 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1067 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1067 host target RNA into VGAM1067 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2460] VGAM1068 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1068 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1068 host target RNA into VGAM1068 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2461] VGAM1069 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1069 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1069 host target RNA into VGAM1069 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2462] VGAM1070 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1070 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1070 host target RNA into VGAM1070 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2463] VGAM1071 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1071 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1071 host target RNA into VGAM1071 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2464] VGAM1072 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1072 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1072 host target RNA into VGAM1072 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2465] VGAM1073 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1073 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1073 host target RNA into VGAM1073 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2466] VGAM1074 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1074 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1074 host target RNA into

VGAM1074 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2467] It is appreciated that a function of VGR2968 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2968 gene include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGR2968 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2968 gene: VGAM1067 host target protein, VGAM1068 host target protein, VGAM1069 host target protein, VGAM1070 host target protein, VGAM1071 host target protein, VGAM1072 host target protein, VGAM1073 host target protein and VGAM1074 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1067, VGAM1068, VGAM1069, VGAM1070, VGAM1071, VGAM1072, VGAM1073 and VGAM1074. Fig.

9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2969(VGR2969) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2468] VGR2969 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2969 gene was detected is described hereinabove with reference to Figs. 1-9.

[2469] VGR2969 gene encodes VGR2969 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2470] VGR2969 precursor RNA folds spatially, forming VGR2969 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2969 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2969 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2471] VGR2969 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1075 precursor RNA, VGAM1076 precursor RNA, VGAM1077 precursor RNA, VGAM1078 precursor RNA, VGAM1079 precursor RNA, VGAM1080 precursor RNA, VGAM1081 precursor RNA and VGAM1082 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2472] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1075 RNA, VGAM1076 RNA, VGAM1077 RNA, VGAM1078 RNA, VGAM1079 RNA, VGAM1080 RNA, VGAM1081 RNA and VGAM1082 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2473] VGAM1075 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1075 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1075 host target RNA into VGAM1075 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2474] VGAM1076 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1076 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1076 host target RNA into VGAM1076 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2475] VGAM1077 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1077 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1077 host target RNA into VGAM1077 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2476] VGAM1078 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1078 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1078 host target RNA into VGAM1078 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2477] VGAM1079 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1079 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1079 host target RNA into VGAM1079 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2478] VGAM1080 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1080 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1080 host target RNA into

VGAM1080 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2479] VGAM1081 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1081 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1081 host target RNA into VGAM1081 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2480] VGAM1082 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1082 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1082 host target RNA into VGAM1082 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2481] It is appreciated that a function of VGR2969 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2969 gene include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGR2969 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2969 gene: VGAM1075 host target protein, VGAM1076 host target protein, VGAM1077 host target protein, VGAM1078 host target protein, VGAM1079 host target protein, VGAM1080 host target protein, VGAM1081 host target protein and VGAM1082 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1075, VGAM1076, VGAM1077, VGAM1078,

VGAM1079, VGAM1080, VGAM1081 and VGAM1082. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2970(VGR2970) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2482] VGR2970 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2970 gene was detected is described hereinabove with reference to Figs. 1-9.

[2483] VGR2970 gene encodes VGR2970 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2484] VGR2970 precursor RNA folds spatially, forming VGR2970 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2970 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR2970 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2485] VGR2970 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1083 precursor RNA, VGAM1084 precursor RNA, VGAM1085 precursor RNA, VGAM1086 precursor RNA, VGAM1087 precursor RNA, VGAM1088 precursor RNA, VGAM1089 precursor RNA and VGAM1090 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2486] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1083 RNA, VGAM1084 RNA, VGAM1085 RNA, VGAM1086 RNA, VGAM1087 RNA, VGAM1088 RNA, VGAM1089 RNA and VGAM1090 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[2487] VGAM1083 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1083 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1083 host target RNA into VGAM1083 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2488] VGAM1084 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1084 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1084 host target RNA into VGAM1084 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2489] VGAM1085 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1085 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1085 host target RNA into VGAM1085 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2490] VGAM1086 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1086 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1086 host target RNA into

VGAM1086 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2491] VGAM1087 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1087 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1087 host target RNA into VGAM1087 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2492] VGAM1088 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1088 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1088 host target RNA into VGAM1088 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2493] VGAM1089 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1089 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1089 host target RNA into VGAM1089 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2494] VGAM1090 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1090 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1090 host target RNA into VGAM1090 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2495] It is appreciated that a function of VGR2970 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2970 gene include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGR2970 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2970 gene: VGAM1083 host target protein, VGAM1084 host target protein, VGAM1085 host target protein, VGAM1086 host target protein, VGAM1087 host target protein, VGAM1088 host target protein, VGAM1089 host target protein and VGAM1090 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with refer-

ence to VGAM1083, VGAM1084, VGAM1085, VGAM1086, VGAM1087, VGAM1088, VGAM1089 and VGAM1090. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2971(VGR2971) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2496] VGR2971 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2971 gene was detected is described hereinabove with reference to Figs. 1-9.

[2497] VGR2971 gene encodes VGR2971 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2498] VGR2971 precursor RNA folds spatially, forming VGR2971 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2971 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR2971 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2499] VGR2971 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1091 precursor RNA, VGAM1092 precursor RNA, VGAM1093 precursor RNA, VGAM1094 precursor RNA and VGAM1095 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2500] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1091 RNA, VGAM1092 RNA, VGAM1093 RNA, VGAM1094 RNA and VGAM1095 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2501] VGAM1091 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1091 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1091 host target RNA into VGAM1091 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2502] VGAM1092 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1092 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1092 host target RNA into VGAM1092 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2503] VGAM1093 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1093 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1093 host target RNA into VGAM1093 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2504] VGAM1094 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1094 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1094 host target RNA into VGAM1094 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2505] VGAM1095 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1095 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1095 host target RNA into VGAM1095 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2506] It is appreciated that a function of VGR2971 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2971 gene include diagnosis, prevention and treatment of viral infection by Poinsettia Mosaic Virus. Specific functions, and accordingly utilities, of VGR2971 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR2971 gene: VGAM1091 host target protein, VGAM1092 host target protein, VGAM1093 host target protein, VGAM1094 host target protein and VGAM1095 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1091, VGAM1092, VGAM1093, VGAM1094 and VGAM1095. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2972(VGR2972) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2507] VGR2972 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2972 gene was detected is described hereinabove with reference to Figs. 1-9.

[2508] VGR2972 gene encodes VGR2972 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2509] VGR2972 precursor RNA folds spatially, forming VGR2972 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2972 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2972 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2510] VGR2972 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1096 precursor RNA, VGAM1097 precursor RNA, VGAM1098 precursor RNA, VGAM1099 precursor RNA, VGAM1100 precursor RNA, VGAM1101 precursor RNA, VGAM1102 precursor RNA and VGAM1103 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2511] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1096 RNA, VGAM1097 RNA, VGAM1098 RNA, VGAM1099 RNA, VGAM1100 RNA, VGAM1101 RNA, VGAM1102 RNA and VGAM1103 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2512] VGAM1096 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1096 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1096 host target RNA into VGAM1096 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2513] VGAM1097 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1097 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1097 host target RNA into VGAM1097 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2514] VGAM1098 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1098 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1098 host target RNA into VGAM1098 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2515] VGAM1099 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1099 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1099 host target RNA into VGAM1099 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2516] VGAM1100 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1100 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1100 host target RNA into VGAM1100 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2517] VGAM1101 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1101 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1101 host target RNA into VGAM1101 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2518] VGAM1102 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1102 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1102 host target RNA into VGAM1102 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2519] VGAM1103 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1103 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1103 host target RNA into VGAM1103 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2520] It is appreciated that a function of VGR2972 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2972 gene include diagnosis, prevention and treatment of viral infection by Strawberry Mottle Virus. Specific functions, and accordingly utilities, of VGR2972 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2972 gene: VGAM1096 host target protein, VGAM1097 host target protein, VGAM1098

host target protein, VGAM1099 host target protein, VGAM1100 host target protein, VGAM1101 host target protein, VGAM1102 host target protein and VGAM1103 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1096, VGAM1097, VGAM1098, VGAM1099, VGAM1100, VGAM1101, VGAM1102 and VGAM1103. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2973 (VGR2973) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2521] VGR2973 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2973 gene was detected is described hereinabove with reference to Figs. 1-9.

[2522] VGR2973 gene encodes VGR2973 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2523] VGR2973 precursor RNA folds spatially, forming VGR2973 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2973 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2973 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2524] VGR2973 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1104 precursor RNA, VGAM1105 precursor RNA and VGAM1106 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2525] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1104 RNA, VGAM1105 RNA and VGAM1106 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2526] VGAM1104 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1104 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1104 host target RNA into VGAM1104 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2527] VGAM1105 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1105 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1105 host target RNA into VGAM1105 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2528] VGAM1106 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1106 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1106 host target RNA into VGAM1106 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2529] It is appreciated that a function of VGR2973 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2973 gene include diagnosis, prevention and treatment of viral infection by

Human Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2973 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2973 gene: VGAM1104 host target protein, VGAM1105 host target protein and VGAM1106 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1104, VGAM1105 and VGAM1106. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2974(VGR2974) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2530] VGR2974 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2974 gene was detected is described hereinabove with reference to Figs.

1-9.

- [2531] VGR2974 gene encodes VGR2974 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2532] VGR2974 precursor RNA folds spatially, forming VGR2974 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2974 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2974 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2533] VGR2974 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1108 precursor RNA and VGAM1109 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2534] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1108 RNA and VGAM1109 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2535] VGAM1108 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1108 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1108 host target RNA into VGAM1108 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2536] VGAM1109 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1109 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1109 host target RNA into VGAM1109 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2537] It is appreciated that a function of VGR2974 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2974 gene include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR2974 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2974 gene: VGAM1108 host target protein and VGAM1109 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1108 and VGAM1109. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 2975(VGR2975) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2538] VGR2975 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2975 gene was detected is described hereinabove with reference to Figs. 1-9.

[2539] VGR2975 gene encodes VGR2975 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2540] VGR2975 precursor RNA folds spatially, forming VGR2975 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2975 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2975 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2541] VGR2975 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1111 precursor RNA, VGAM1112 precursor RNA, VGAM1113 precursor RNA, VGAM1114 precursor RNA and VGAM1115 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2542] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1111 RNA, VGAM1112 RNA, VGAM1113 RNA, VGAM1114 RNA and VGAM1115 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2543] VGAM1111 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1111 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1111 host target RNA into VGAM1111 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2544] VGAM1112 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1112 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1112 host target RNA into VGAM1112 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2545] VGAM1113 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1113 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1113 host target RNA into VGAM1113 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2546] VGAM1114 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1114 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1114 host target RNA into VGAM1114 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2547] VGAM1115 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1115 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1115 host target RNA into VGAM1115 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2548] It is appreciated that a function of VGR2975 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2975 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR2975 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2975 gene: VGAM1111 host target protein, VGAM1112 host target protein, VGAM1113 host target protein, VGAM1114 host target protein and

VGAM1115 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1111, VGAM1112, VGAM1113, VGAM1114 and VGAM1115. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2976(VGR2976) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2549] VGR2976 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2976 gene was detected is described hereinabove with reference to Figs. 1-9.

[2550] VGR2976 gene encodes VGR2976 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2551] VGR2976 precursor RNA folds spatially, forming VGR2976 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR2976 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2976 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2552] VGR2976 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1116 precursor RNA, VGAM1117 precursor RNA, VGAM1118 precursor RNA, VGAM1119 precursor RNA and VGAM1120 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2553] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1116 RNA, VGAM1117 RNA, VGAM1118 RNA, VGAM1119 RNA

and VGAM1120 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2554] VGAM1116 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1116 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1116 host target RNA into VGAM1116 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2555] VGAM1117 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1117 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1117 host target RNA into VGAM1117 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2556] VGAM1118 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1118 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1118 host target RNA into VGAM1118 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2557] VGAM1119 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1119 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1119 host target RNA into VGAM1119 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2558] VGAM1120 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1120 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1120 host target RNA into VGAM1120 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2559] It is appreciated that a function of VGR2976 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2976 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly util-

ities, of VGR2976 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2976 gene: VGAM1116 host target protein, VGAM1117 host target protein, VGAM1118 host target protein, VGAM1119 host target protein and VGAM1120 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1116, VGAM1117, VGAM1118, VGAM1119 and VGAM1120. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2977(VGR2977) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2560] VGR2977 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2977 gene was detected is described hereinabove with reference to Figs.

1-9.

[2561] VGR2977 gene encodes VGR2977 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2562] VGR2977 precursor RNA folds spatially, forming VGR2977 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2977 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2977 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2563] VGR2977 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1121 precursor RNA, VGAM1122 precursor RNA, VGAM1123 precursor RNA, VGAM1124 precursor RNA and VGAM1125 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2564] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1121 RNA, VGAM1122 RNA, VGAM1123 RNA, VGAM1124 RNA and VGAM1125 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2565] VGAM1121 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1121 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1121 host target RNA into VGAM1121 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2566] VGAM1122 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1122 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1122 host target RNA into VGAM1122 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2567] VGAM1123 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1123 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1123 host target RNA into VGAM1123 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2568] VGAM1124 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1124 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1124 host target RNA into VGAM1124 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2569] VGAM1125 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1125 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1125 host target RNA into VGAM1125 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2570] It is appreciated that a function of VGR2977 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2977 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR2977 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2977 gene: VGAM1121 host target protein, VGAM1122 host target protein, VGAM1123 host target protein, VGAM1124 host target protein and VGAM1125 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1121, VGAM1122, VGAM1123, VGAM1124 and VGAM1125. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2978(VGR2978) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[2571] VGR2978 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2978 gene was detected is described hereinabove with reference to Figs. 1-9.

[2572] VGR2978 gene encodes VGR2978 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2573] VGR2978 precursor RNA folds spatially, forming VGR2978 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2978 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2978 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2574] VGR2978 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM

precursor RNAs, VGAM1127 precursor RNA, VGAM1128 precursor RNA, VGAM1129 precursor RNA, VGAM1130 precursor RNA, VGAM1131 precursor RNA and VGAM1132 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2575] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1127 RNA, VGAM1128 RNA, VGAM1129 RNA, VGAM1130 RNA, VGAM1131 RNA and VGAM1132 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2576] VGAM1127 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1127 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1127 host target RNA into VGAM1127 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2577] VGAM1128 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1128 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1128 host target RNA into VGAM1128 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2578] VGAM1129 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1129 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1129 host target RNA into VGAM1129 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2579] VGAM1130 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1130 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1130 host target RNA into VGAM1130 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2580] VGAM1131 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1131 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1131 host target RNA into VGAM1131 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2581] VGAM1132 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1132 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1132 host target RNA into VGAM1132 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2582] It is appreciated that a function of VGR2978 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2978 gene include

diagnosis, prevention and treatment of viral infection by Barley Stripe Mosaic Virus. Specific functions, and accordingly utilities, of VGR2978 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2978 gene: VGAM1127 host target protein, VGAM1128 host target protein, VGAM1129 host target protein, VGAM1130 host target protein, VGAM1131 host target protein and VGAM1132 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1127, VGAM1128, VGAM1129, VGAM1130, VGAM1131 and VGAM1132. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2979(VGR2979) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2583] VGR2979 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2979 gene was detected is described hereinabove with reference to Figs. 1-9.

[2584] VGR2979 gene encodes VGR2979 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2585] VGR2979 precursor RNA folds spatially, forming VGR2979 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2979 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2979 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2586] VGR2979 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1133 precursor RNA, VGAM1134 precursor RNA and VGAM1135 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2587] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1133 RNA, VGAM1134 RNA and VGAM1135 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2588] VGAM1133 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1133 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1133 host target RNA into VGAM1133 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2589] VGAM1134 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1134 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1134 host target RNA into VGAM1134 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2590] VGAM1135 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1135 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1135 host target RNA into VGAM1135 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2591] It is appreciated that a function of VGR2979 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2979 gene include diagnosis, prevention and treatment of viral infection by Maize Rayado Fino Virus. Specific functions, and accordingly utilities, of VGR2979 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2979 gene: VGAM1133 host target protein, VGAM1134 host target protein and VGAM1135 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1133, VGAM1134 and VGAM1135. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2980(VGR2980) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[2592] VGR2980 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2980 gene was detected is described hereinabove with reference to Figs. 1-9.

[2593] VGR2980 gene encodes VGR2980 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2594] VGR2980 precursor RNA folds spatially, forming VGR2980 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2980 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2980 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2595] VGR2980 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM1136 precursor RNA, VGAM1137 precursor RNA and VGAM1138 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2596] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1136 RNA, VGAM1137 RNA and VGAM1138 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2597] VGAM1136 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1136 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1136 host target RNA into

VGAM1136 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2598] VGAM1137 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1137 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1137 host target RNA into VGAM1137 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2599] VGAM1138 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1138 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1138 host target RNA into VGAM1138 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2600] It is appreciated that a function of VGR2980 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2980 gene include diagnosis, prevention and treatment of viral infection by Beet Mild Yellowing Virus. Specific functions, and accordingly utilities, of VGR2980 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2980 gene: VGAM1136 host target protein, VGAM1137 host target protein and VGAM1138 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1136, VGAM1137 and VGAM1138. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2981(VGR2981) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2601] VGR2981 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2981 gene was detected is described hereinabove with reference to Figs. 1-9.

[2602] VGR2981 gene encodes VGR2981 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2603] VGR2981 precursor RNA folds spatially, forming VGR2981 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2981 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2981 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[2604] VGR2981 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1139 precursor RNA, VGAM1140 precursor RNA and VGAM1141 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2605] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1139 RNA, VGAM1140 RNA and VGAM1141 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2606] VGAM1139 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1139 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1139 host target RNA into VGAM1139 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2607] VGAM1140 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1140 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1140 host target RNA into VGAM1140 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2608] VGAM1141 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1141 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1141 host target RNA into VGAM1141 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2609] It is appreciated that a function of VGR2981 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2981 gene include diagnosis, prevention and treatment of viral infection by Chayote Mosaic Tymovirus. Specific functions, and accordingly utilities, of VGR2981 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2981 gene: VGAM1139 host target protein, VGAM1140 host target protein and VGAM1141 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1139, VGAM1140 and VGAM1141. Fig. 9

further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2982(VGR2982) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2610] VGR2982 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2982 gene was detected is described hereinabove with reference to Figs. 1-9.

[2611] VGR2982 gene encodes VGR2982 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2612] VGR2982 precursor RNA folds spatially, forming VGR2982 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2982 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2982 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2613] VGR2982 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1142 precursor RNA, VGAM1143 precursor RNA, VGAM1144 precursor RNA and VGAM1145 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2614] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1142 RNA, VGAM1143 RNA, VGAM1144 RNA and VGAM1145 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2615] VGAM1142 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1142 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1142 host target RNA into VGAM1142 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2616] VGAM1143 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1143 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1143 host target RNA into VGAM1143 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2617] VGAM1144 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1144 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1144 host target RNA into VGAM1144 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2618] VGAM1145 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1145 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1145 host target RNA into VGAM1145 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2619] It is appreciated that a function of VGR2982 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2982 gene include diagnosis, prevention and treatment of viral infection by Bamboo Mosaic Virus. Specific functions, and accordingly utilities, of VGR2982 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2982 gene: VGAM1142 host target protein, VGAM1143 host target protein, VGAM1144 host target protein and VGAM1145 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1142, VGAM1143, VGAM1144 and VGAM1145. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2983(VGR2983) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2620] VGR2983 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2983 gene was detected is described hereinabove with reference to Figs. 1–9.

[2621] VGR2983 gene encodes VGR2983 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2622] VGR2983 precursor RNA folds spatially, forming VGR2983 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2983 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2983 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[2623] VGR2983 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1146 precursor RNA and VGAM1147 precursor RNA, herein schematically repre–

sented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2624] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1146 RNA and VGAM1147 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2625] VGAM1146 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1146 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1146 host target RNA into VGAM1146 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2626] VGAM1147 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1147 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1147 host target RNA into VGAM1147 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2627] It is appreciated that a function of VGR2983 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2983 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR2983 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2983 gene: VGAM1146 host target protein and VGAM1147 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1146 and VGAM1147. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2984(VGR2984) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2628] VGR2984 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2984 gene was detected is described hereinabove with reference to Figs. 1-9.

[2629] VGR2984 gene encodes VGR2984 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2630] VGR2984 precursor RNA folds spatially, forming VGR2984 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2984 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2984 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2631] VGR2984 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1148 precursor RNA, VGAM1149 precursor RNA and VGAM1150 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2632] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1148 RNA, VGAM1149 RNA and VGAM1150 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2633] VGAM1148 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1148 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1148 host target RNA into VGAM1148 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2634] VGAM1149 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1149 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1149 host target RNA into VGAM1149 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2635] VGAM1150 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1150 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1150 host target RNA into VGAM1150 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2636] It is appreciated that a function of VGR2984 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2984 gene include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR2984 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2984 gene: VGAM1148

host target protein, VGAM1149 host target protein and VGAM1150 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1148, VGAM1149 and VGAM1150. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2985(VGR2985) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2637] VGR2985 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2985 gene was detected is described hereinabove with reference to Figs. 1-9.

[2638] VGR2985 gene encodes VGR2985 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2639] VGR2985 precursor RNA folds spatially, forming VGR2985

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2985 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2985 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2640] VGR2985 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1151 precursor RNA, VGAM1152 precursor RNA, VGAM1153 precursor RNA and VGAM1154 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2641] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1151 RNA, VGAM1152 RNA, VGAM1153 RNA and VGAM1154

RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2642] VGAM1151 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1151 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1151 host target RNA into VGAM1151 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2643] VGAM1152 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1152 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1152 host target RNA into VGAM1152 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2644] VGAM1153 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1153 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1153 host target RNA into VGAM1153 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2645] VGAM1154 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1154 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1154 host target RNA into VGAM1154 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2646] It is appreciated that a function of VGR2985 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2985 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR2985 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2985 gene: VGAM1151 host target protein, VGAM1152 host target protein, VGAM1153 host target protein and VGAM1154 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1151, VGAM1152, VGAM1153 and VGAM1154. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral

gene, referred to here as Viral Genomic Record 2986(VGR2986) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2647] VGR2986 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2986 gene was detected is described hereinabove with reference to Figs. 1-9.

[2648] VGR2986 gene encodes VGR2986 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2649] VGR2986 precursor RNA folds spatially, forming VGR2986 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2986 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2986 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[2650] VGR2986 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1155 precursor RNA, VGAM1156 precursor RNA and VGAM1157 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2651] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1155 RNA, VGAM1156 RNA and VGAM1157 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2652] VGAM1155 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1155 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1155 host target RNA into VGAM1155 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2653] VGAM1156 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1156 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1156 host target RNA into VGAM1156 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2654] VGAM1157 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1157 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1157 host target RNA into VGAM1157 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2655] It is appreciated that a function of VGR2986 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2986 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR2986 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2986 gene: VGAM1155 host target protein, VGAM1156 host target protein and VGAM1157 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1155, VGAM1156 and

VGAM1157. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2987 (VGR2987) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2656] VGR2987 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2987 gene was detected is described hereinabove with reference to Figs. 1-9.

[2657] VGR2987 gene encodes VGR2987 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2658] VGR2987 precursor RNA folds spatially, forming VGR2987 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2987 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2987 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2659] VGR2987 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1159 precursor RNA, VGAM1160 precursor RNA and VGAM1161 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2660] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1159 RNA, VGAM1160 RNA and VGAM1161 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2661] VGAM1159 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1159 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1159 host target RNA into VGAM1159 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2662] VGAM1160 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1160 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1160 host target RNA into VGAM1160 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2663] VGAM1161 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1161 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1161 host target RNA into VGAM1161 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2664] It is appreciated that a function of VGR2987 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2987 gene include diagnosis, prevention and treatment of viral infection by Meleagrid Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2987 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2987 gene: VGAM1159 host target protein, VGAM1160 host target protein and VGAM1161 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1159, VGAM1160 and VGAM1161. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2988(VGR2988) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2665] VGR2988 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2988 gene was detected is described hereinabove with reference to Figs. 1-9.

[2666] VGR2988 gene encodes VGR2988 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2667] VGR2988 precursor RNA folds spatially, forming VGR2988 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2988 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2988 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2668] VGR2988 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1162 precursor RNA, VGAM1163 precursor RNA, VGAM1164 precursor RNA and VGAM1165 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2669] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1162 RNA, VGAM1163 RNA, VGAM1164 RNA and VGAM1165 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2670] VGAM1162 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1162 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1162 host target RNA into VGAM1162 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2671] VGAM1163 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1163 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1163 host target RNA into VGAM1163 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2672] VGAM1164 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1164 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1164 host target RNA into VGAM1164 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2673] VGAM1165 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1165 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1165 host target RNA into VGAM1165 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2674] It is appreciated that a function of VGR2988 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2988 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR2988 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2988 gene: VGAM1162 host target protein, VGAM1163 host target protein, VGAM1164 host target protein and VGAM1165 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1162, VGAM1163, VGAM1164 and VGAM1165. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2989(VGR2989) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2675] VGR2989 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2989 gene was detected is described hereinabove with reference to Figs. 1-9.

[2676] VGR2989 gene encodes VGR2989 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2677] VGR2989 precursor RNA folds spatially, forming VGR2989 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2989 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2989 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2678] VGR2989 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1166 precursor RNA and VGAM1167 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2679] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1166 RNA and VGAM1167 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2680] VGAM1166 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1166 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1166 host target RNA into VGAM1166 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2681] VGAM1167 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1167 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1167 host target RNA into VGAM1167 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2682] It is appreciated that a function of VGR2989 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2989 gene include diagnosis, prevention and treatment of viral infection by Cucumber Green Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGR2989 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in

the `operon-like` cluster of VGR2989 gene: VGAM1166 host target protein and VGAM1167 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1166 and VGAM1167. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2990(VGR2990) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2683] VGR2990 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2990 gene was detected is described hereinabove with reference to Figs. 1-9.

[2684] VGR2990 gene encodes VGR2990 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2685] VGR2990 precursor RNA folds spatially, forming VGR2990

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2990 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2990 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2686] VGR2990 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1168 precursor RNA and VGAM1169 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2687] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1168 RNA and VGAM1169 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2688] VGAM1168 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1168 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1168 host target RNA into VGAM1168 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2689] VGAM1169 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1169 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1169 host target RNA into VGAM1169 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2690] It is appreciated that a function of VGR2990 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2990 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR2990 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2990 gene: VGAM1168 host target protein and VGAM1169 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1168 and VGAM1169. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2991(VGR2991) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[2691] VGR2991 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2991 gene was detected is described hereinabove with reference to Figs. 1-9.

[2692] VGR2991 gene encodes VGR2991 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2693] VGR2991 precursor RNA folds spatially, forming VGR2991 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2991 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2991 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2694] VGR2991 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM1171 precursor RNA, VGAM1172 precursor RNA and VGAM1173 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2695] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1171 RNA, VGAM1172 RNA and VGAM1173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2696] VGAM1171 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1171 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1171 host target RNA into

VGAM1171 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2697] VGAM1172 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1172 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1172 host target RNA into VGAM1172 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2698] VGAM1173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1173 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1173 host target RNA into VGAM1173 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2699] It is appreciated that a function of VGR2991 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2991 gene include diagnosis, prevention and treatment of viral infection by Cucumber Fruit Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGR2991 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2991 gene: VGAM1171 host target protein, VGAM1172 host target protein and VGAM1173 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1171, VGAM1172 and VGAM1173. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2992(VGR2992) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2700] VGR2992 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2992 gene was detected is described hereinabove with reference to Figs. 1-9.

[2701] VGR2992 gene encodes VGR2992 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2702] VGR2992 precursor RNA folds spatially, forming VGR2992 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2992 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2992 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[2703] VGR2992 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1174 precursor RNA, VGAM1175 precursor RNA and VGAM1176 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2704] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1174 RNA, VGAM1175 RNA and VGAM1176 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2705] VGAM1174 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1174 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1174 host target RNA into VGAM1174 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2706] VGAM1175 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1175 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1175 host target RNA into VGAM1175 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2707] VGAM1176 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1176 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1176 host target RNA into VGAM1176 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2708] It is appreciated that a function of VGR2992 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2992 gene include diagnosis, prevention and treatment of viral infection by Rift Valley Fever Virus. Specific functions, and accordingly utilities, of VGR2992 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2992 gene: VGAM1174 host target protein, VGAM1175 host target protein and VGAM1176 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1174, VGAM1175 and VGAM1176. Fig. 9

further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2993(VGR2993) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2709] VGR2993 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2993 gene was detected is described hereinabove with reference to Figs. 1-9.

[2710] VGR2993 gene encodes VGR2993 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2711] VGR2993 precursor RNA folds spatially, forming VGR2993 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2993 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2993 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2712] VGR2993 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1177 precursor RNA, VGAM1178 precursor RNA, VGAM1179 precursor RNA, VGAM1180 precursor RNA and VGAM1181 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2713] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1177 RNA, VGAM1178 RNA, VGAM1179 RNA, VGAM1180 RNA and VGAM1181 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2714] VGAM1177 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1177 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1177 host target RNA into VGAM1177 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2715] VGAM1178 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1178 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1178 host target RNA into VGAM1178 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2716] VGAM1179 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1179 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1179 host target RNA into VGAM1179 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2717] VGAM1180 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1180 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1180 host target RNA into VGAM1180 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2718] VGAM1181 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1181 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1181 host target RNA into VGAM1181 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2719] It is appreciated that a function of VGR2993 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2993 gene include diagnosis, prevention and treatment of viral infection by Odontoglossum Ringspot Virus. Specific functions, and accordingly utilities, of VGR2993 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2993 gene: VGAM1177 host target protein, VGAM1178 host target protein,

VGAM1179 host target protein, VGAM1180 host target protein and VGAM1181 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1177, VGAM1178, VGAM1179, VGAM1180 and VGAM1181. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2994(VGR2994) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2720] VGR2994 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2994 gene was detected is described hereinabove with reference to Figs. 1-9.

[2721] VGR2994 gene encodes VGR2994 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2722] VGR2994 precursor RNA folds spatially, forming VGR2994

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2994 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2994 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2723] VGR2994 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1183 precursor RNA, VGAM1184 precursor RNA and VGAM1185 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2724] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1183 RNA, VGAM1184 RNA and VGAM1185 RNA, herein

schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2725] VGAM1183 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1183 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1183 host target RNA into VGAM1183 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2726] VGAM1184 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1184 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1184 host target RNA into VGAM1184 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2727] VGAM1185 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1185 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1185 host target RNA into VGAM1185 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2728] It is appreciated that a function of VGR2994 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2994 gene include diagnosis, prevention and treatment of viral infection by Cactus Virus X. Specific functions, and accordingly utilities, of VGR2994 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2994 gene: VGAM1183 host target protein, VGAM1184 host target protein and VGAM1185 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1183, VGAM1184 and VGAM1185. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2995(VGR2995) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2729] VGR2995 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2995 gene was detected is described hereinabove with reference to Figs. 1-9.

[2730] VGR2995 gene encodes VGR2995 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2731] VGR2995 precursor RNA folds spatially, forming VGR2995 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2995 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2995 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2732] VGR2995 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1186 precursor RNA, VGAM1187 precursor RNA and VGAM1188 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2733] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1186 RNA, VGAM1187 RNA and VGAM1188 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2734] VGAM1186 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1186 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1186 host target RNA into VGAM1186 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2735] VGAM1187 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1187 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1187 host target RNA into VGAM1187 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2736] VGAM1188 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1188 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1188 host target RNA into VGAM1188 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2737] It is appreciated that a function of VGR2995 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2995 gene include

diagnosis, prevention and treatment of viral infection by Human Adenovirus C. Specific functions, and accordingly utilities, of VGR2995 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2995 gene: VGAM1186 host target protein, VGAM1187 host target protein and VGAM1188 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1186, VGAM1187 and VGAM1188. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2996(VGR2996) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2738] VGR2996 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2996 gene was

detected is described hereinabove with reference to Figs. 1-9.

[2739] VGR2996 gene encodes VGR2996 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2740] VGR2996 precursor RNA folds spatially, forming VGR2996 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2996 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2996 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2741] VGR2996 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1189 precursor RNA, VGAM1190 precursor RNA and VGAM1191 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2742] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1189 RNA, VGAM1190 RNA and VGAM1191 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2743] VGAM1189 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1189 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1189 host target RNA into VGAM1189 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2744] VGAM1190 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1190 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1190 host target RNA into VGAM1190 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2745] VGAM1191 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1191 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1191 host target RNA into VGAM1191 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2746] It is appreciated that a function of VGR2996 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2996 gene include diagnosis, prevention and treatment of viral infection by Botrytis Virus F. Specific functions, and accordingly utilities, of VGR2996 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2996 gene: VGAM1189 host target protein, VGAM1190 host target protein and VGAM1191 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1189, VGAM1190 and VGAM1191. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2997(VGR2997) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2747] VGR2997 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2997 gene was detected is described hereinabove with reference to Figs. 1-9.

[2748] VGR2997 gene encodes VGR2997 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2749] VGR2997 precursor RNA folds spatially, forming VGR2997 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2997 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2997 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2750] VGR2997 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1192 precursor RNA, VGAM1193 precursor RNA and VGAM1194 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2751] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1192 RNA, VGAM1193 RNA and VGAM1194 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2752] VGAM1192 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1192 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1192 host target RNA into VGAM1192 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2753] VGAM1193 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1193 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1193 host target RNA into VGAM1193 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2754] VGAM1194 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1194 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1194 host target RNA into VGAM1194 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2755] It is appreciated that a function of VGR2997 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2997 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR2997 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2997 gene: VGAM1192 host target protein, VGAM1193 host target protein and VGAM1194 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1192, VGAM1193 and VGAM1194. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2998(VGR2998) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[2756] VGR2998 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2998 gene was detected is described hereinabove with reference to Figs. 1-9.

[2757] VGR2998 gene encodes VGR2998 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2758] VGR2998 precursor RNA folds spatially, forming VGR2998 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2998 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2998 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2759] VGR2998 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM

precursor RNAs, VGAM1195 precursor RNA, VGAM1196 precursor RNA, VGAM1197 precursor RNA and VGAM1198 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2760] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1195 RNA, VGAM1196 RNA, VGAM1197 RNA and VGAM1198 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2761] VGAM1195 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1195 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1195 host target RNA into

VGAM1195 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2762] VGAM1196 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1196 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1196 host target RNA into VGAM1196 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2763] VGAM1197 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1197 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1197 host target RNA into VGAM1197 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2764] VGAM1198 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1198 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1198 host target RNA into VGAM1198 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2765] It is appreciated that a function of VGR2998 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2998 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR2998 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2998 gene: VGAM1195 host target protein, VGAM1196 host target protein, VGAM1197 host target protein and VGAM1198 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1195, VGAM1196, VGAM1197 and VGAM1198. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 2999(VGR2999) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2766] VGR2999 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR2999 gene was detected is described hereinabove with reference to Figs. 1-9.

[2767] VGR2999 gene encodes VGR2999 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2768] VGR2999 precursor RNA folds spatially, forming VGR2999 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR2999 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR2999 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2769] VGR2999 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1199 precursor RNA, VGAM1200 precursor RNA, VGAM1201 precursor RNA and VGAM1202 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2770] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1199 RNA, VGAM1200 RNA, VGAM1201 RNA and VGAM1202 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2771] VGAM1199 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1199 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1199 host target RNA into VGAM1199 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2772] VGAM1200 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1200 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1200 host target RNA into VGAM1200 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2773] VGAM1201 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1201 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1201 host target RNA into VGAM1201 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2774] VGAM1202 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1202 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1202 host target RNA into VGAM1202 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2775] It is appreciated that a function of VGR2999 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR2999 gene include diagnosis, prevention and treatment of viral infection by Avian Nephritis Virus. Specific functions, and accordingly utilities, of VGR2999 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR2999 gene: VGAM1199 host target protein, VGAM1200 host target protein, VGAM1201 host target protein and VGAM1202 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-

above with reference to VGAM1199, VGAM1200, VGAM1201 and VGAM1202. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3000 (VGR3000) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2776] VGR3000 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3000 gene was detected is described hereinabove with reference to Figs. 1-9.

[2777] VGR3000 gene encodes VGR3000 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2778] VGR3000 precursor RNA folds spatially, forming VGR3000 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3000 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3000 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2779] VGR3000 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1203 precursor RNA, VGAM1204 precursor RNA and VGAM1205 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2780] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1203 RNA, VGAM1204 RNA and VGAM1205 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2781] VGAM1203 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1203 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1203 host target RNA into VGAM1203 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2782] VGAM1204 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1204 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1204 host target RNA into VGAM1204 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2783] VGAM1205 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1205 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1205 host target RNA into VGAM1205 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2784] It is appreciated that a function of VGR3000 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3000 gene include diagnosis, prevention and treatment of viral infection by Scallion Virus X. Specific functions, and accordingly utilities, of VGR3000 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3000 gene: VGAM1203 host target protein, VGAM1204 host target protein and VGAM1205 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1203, VGAM1204 and VGAM1205. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3001(VGR3001) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2785] VGR3001 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3001 gene was detected is described hereinabove with reference to Figs. 1-9.

[2786] VGR3001 gene encodes VGR3001 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2787] VGR3001 precursor RNA folds spatially, forming VGR3001 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3001 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3001 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2788] VGR3001 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1206 precursor RNA, VGAM1207 precursor RNA, VGAM1208 precursor RNA and VGAM1209 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2789] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1206 RNA, VGAM1207 RNA, VGAM1208 RNA and VGAM1209 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corre-

sponding to VGAM RNA of Fig. 1.

[2790] VGAM1206 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1206 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1206 host target RNA into VGAM1206 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2791] VGAM1207 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1207 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1207 host target RNA into VGAM1207 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2792] VGAM1208 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1208 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1208 host target RNA into VGAM1208 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2793] VGAM1209 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1209 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1209 host target RNA into

VGAM1209 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2794] It is appreciated that a function of VGR3001 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3001 gene include diagnosis, prevention and treatment of viral infection by Clover Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGR3001 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3001 gene: VGAM1206 host target protein, VGAM1207 host target protein, VGAM1208 host target protein and VGAM1209 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1206, VGAM1207, VGAM1208 and VGAM1209. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3002(VGR3002) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2795] VGR3002 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3002 gene was detected is described hereinabove with reference to Figs. 1-9.

[2796] VGR3002 gene encodes VGR3002 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2797] VGR3002 precursor RNA folds spatially, forming VGR3002 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3002 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3002 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2798] VGR3002 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1210 precursor RNA, VGAM1211 precursor RNA and VGAM1212 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2799] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1210 RNA, VGAM1211 RNA and VGAM1212 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2800] VGAM1210 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1210 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1210 host target RNA into VGAM1210 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2801] VGAM1211 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1211 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1211 host target RNA into VGAM1211 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2802] VGAM1212 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1212 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1212 host target RNA into VGAM1212 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2803] It is appreciated that a function of VGR3002 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3002 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3002 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3002 gene: VGAM1210 host target protein, VGAM1211 host target protein and VGAM1212 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1210, VGAM1211 and VGAM1212. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 3003(VGR3003) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2804] VGR3003 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3003 gene was detected is described hereinabove with reference to Figs. 1-9.

[2805] VGR3003 gene encodes VGR3003 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2806] VGR3003 precursor RNA folds spatially, forming VGR3003 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3003 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3003 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2807] VGR3003 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1214 precursor RNA, VGAM1215 precursor RNA, VGAM1216 precursor RNA and VGAM1217 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2808] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1214 RNA, VGAM1215 RNA, VGAM1216 RNA and VGAM1217 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2809] VGAM1214 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1214 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1214 host target RNA into VGAM1214 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2810] VGAM1215 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1215 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1215 host target RNA into VGAM1215 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2811] VGAM1216 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1216 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1216 host target RNA into VGAM1216 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2812] VGAM1217 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1217 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1217 host target RNA into VGAM1217 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2813] It is appreciated that a function of VGR3003 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3003 gene include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGR3003 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3003 gene: VGAM1214 host target protein, VGAM1215 host target protein, VGAM1216 host target protein and VGAM1217 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1214, VGAM1215, VGAM1216 and VGAM1217. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3004(VGR3004) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2814] VGR3004 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3004 gene was detected is described hereinabove with reference to Figs. 1-9.

[2815] VGR3004 gene encodes VGR3004 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2816] VGR3004 precursor RNA folds spatially, forming VGR3004 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3004 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3004 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2817] VGR3004 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1218 precursor RNA and VGAM1219 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3

FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2818] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1218 RNA and VGAM1219 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2819] VGAM1218 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1218 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1218 host target RNA into VGAM1218 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2820] VGAM1219 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1219 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1219 host target RNA into VGAM1219 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2821] It is appreciated that a function of VGR3004 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3004 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3004 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3004 gene: VGAM1218 host target protein and VGAM1219 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM1218 and VGAM1219. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3005 (VGR3005) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2822] VGR3005 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3005 gene was detected is described hereinabove with reference to Figs. 1-9.

[2823] VGR3005 gene encodes VGR3005 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2824] VGR3005 precursor RNA folds spatially, forming VGR3005 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3005 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3005 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2825] VGR3005 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1220 precursor RNA, VGAM1221 precursor RNA and VGAM1222 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2826] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1220 RNA, VGAM1221 RNA and VGAM1222 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2827] VGAM1220 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1220 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1220 host target RNA into VGAM1220 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2828] VGAM1221 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1221 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1221 host target RNA into VGAM1221 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2829] VGAM1222 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1222 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1222 host target RNA into VGAM1222 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2830] It is appreciated that a function of VGR3005 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3005 gene include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGR3005 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3005 gene: VGAM1220 host target protein, VGAM1221 host target protein and

VGAM1222 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1220, VGAM1221 and VGAM1222. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3006(VGR3006) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2831] VGR3006 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3006 gene was detected is described hereinabove with reference to Figs. 1-9.

[2832] VGR3006 gene encodes VGR3006 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2833] VGR3006 precursor RNA folds spatially, forming VGR3006 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3006 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3006 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2834] VGR3006 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1223 precursor RNA and VGAM1224 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2835] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1223 RNA and VGAM1224 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2836] VGAM1223 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1223 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1223 host target RNA into VGAM1223 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2837] VGAM1224 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1224 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1224 host target RNA into VGAM1224 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2838] It is appreciated that a function of VGR3006 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3006 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3006 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3006 gene: VGAM1223 host target protein and VGAM1224 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1223 and VGAM1224. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3007(VGR3007) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in

the art.

[2839] VGR3007 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3007 gene was detected is described hereinabove with reference to Figs. 1-9.

[2840] VGR3007 gene encodes VGR3007 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2841] VGR3007 precursor RNA folds spatially, forming VGR3007 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3007 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3007 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2842] VGR3007 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1226 precursor RNA, VGAM1227

precursor RNA, VGAM1228 precursor RNA and VGAM1229 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2843] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1226 RNA, VGAM1227 RNA, VGAM1228 RNA and VGAM1229 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2844] VGAM1226 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1226 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1226 host target RNA into VGAM1226 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2845] VGAM1227 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1227 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1227 host target RNA into VGAM1227 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2846] VGAM1228 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1228 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1228 host target RNA into

VGAM1228 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2847] VGAM1229 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1229 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1229 host target RNA into VGAM1229 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2848] It is appreciated that a function of VGR3007 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3007 gene include diagnosis, prevention and treatment of viral infection by Tacaribe Virus. Specific functions, and accordingly utilities, of VGR3007 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3007 gene: VGAM1226 host
target protein, VGAM1227 host target protein, VGAM1228
host target protein and VGAM1229 host target protein,
herein schematically represented by VGAM1 HOST TARGET
PROTEIN through VGAM3 HOST TARGET PROTEIN. The
function of these host target genes is elaborated herein-
above with reference to VGAM1226, VGAM1227,
VGAM1228 and VGAM1229. Fig. 9 further provides a con-
ceptual description of novel bioinformatically detected
regulatory viral gene, referred to here as Viral Genomic
Record 3008(VGR3008) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[2849] VGR3008 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3008 gene was
detected is described hereinabove with reference to Figs.
1-9.

[2850] VGR3008 gene encodes VGR3008 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[2851] VGR3008 precursor RNA folds spatially, forming VGR3008 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3008 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3008 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2852] VGR3008 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1230 precursor RNA, VGAM1231 precursor RNA, VGAM1232 precursor RNA, VGAM1233 precursor RNA and VGAM1234 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2853] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1230 RNA, VGAM1231 RNA, VGAM1232 RNA, VGAM1233 RNA and VGAM1234 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2854] VGAM1230 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1230 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1230 host target RNA into VGAM1230 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2855] VGAM1231 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1231 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1231 host target RNA into VGAM1231 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2856] VGAM1232 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1232 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1232 host target RNA into VGAM1232 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2857] VGAM1233 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1233 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1233 host target RNA into VGAM1233 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2858] VGAM1234 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1234 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1234 host target RNA into VGAM1234 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2859] It is appreciated that a function of VGR3008 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3008 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3008 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3008 gene: VGAM1230 host target protein, VGAM1231 host target protein, VGAM1232 host target protein, VGAM1233 host target protein and VGAM1234 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1230, VGAM1231, VGAM1232, VGAM1233 and VGAM1234. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3009(VGR3009) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2860] VGR3009 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3009 gene was detected is described hereinabove with reference to Figs. 1-9.

[2861] VGR3009 gene encodes VGR3009 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2862] VGR3009 precursor RNA folds spatially, forming VGR3009 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3009 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3009 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2863] VGR3009 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1235 precursor RNA, VGAM1236 precursor RNA, VGAM1237 precursor RNA, VGAM1238 precursor RNA, VGAM1239 precursor RNA and VGAM1240

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2864] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1235 RNA, VGAM1236 RNA, VGAM1237 RNA, VGAM1238 RNA, VGAM1239 RNA and VGAM1240 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2865] VGAM1235 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1235 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1235 host target RNA into VGAM1235 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2866] VGAM1236 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1236 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1236 host target RNA into VGAM1236 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2867] VGAM1237 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1237 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1237 host target RNA into

VGAM1237 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2868] VGAM1238 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1238 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1238 host target RNA into VGAM1238 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2869] VGAM1239 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1239 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1239 host target RNA into VGAM1239 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2870] VGAM1240 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1240 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1240 host target RNA into VGAM1240 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2871] It is appreciated that a function of VGR3009 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3009 gene include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3009 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3009 gene: VGAM1235 host target protein, VGAM1236 host target protein, VGAM1237 host target protein, VGAM1238 host target protein, VGAM1239 host target protein and VGAM1240 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1235, VGAM1236, VGAM1237, VGAM1238, VGAM1239 and VGAM1240. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3010(VGR3010) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2872] VGR3010 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3010 gene was detected is described hereinabove with reference to Figs.

1-9.

- [2873] VGR3010 gene encodes VGR3010 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2874] VGR3010 precursor RNA folds spatially, forming VGR3010 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3010 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3010 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2875] VGR3010 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1241 precursor RNA and VGAM1242 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2876] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1241 RNA and VGAM1242 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2877] VGAM1241 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1241 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1241 host target RNA into VGAM1241 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2878] VGAM1242 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1242 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1242 host target RNA into VGAM1242 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2879] It is appreciated that a function of VGR3010 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3010 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3010 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3010 gene: VGAM1241 host target protein and VGAM1242 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1241 and VGAM1242. Fig. 9 further provides a conceptual description of novel bioinfor-

matically detected regulatory viral gene, referred to here as Viral Genomic Record 3011(VGR3011) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2880] VGR3011 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3011 gene was detected is described hereinabove with reference to Figs. 1-9.

[2881] VGR3011 gene encodes VGR3011 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2882] VGR3011 precursor RNA folds spatially, forming VGR3011 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3011 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3011 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2883] VGR3011 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1243 precursor RNA, VGAM1244 precursor RNA, VGAM1245 precursor RNA and VGAM1246 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2884] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1243 RNA, VGAM1244 RNA, VGAM1245 RNA and VGAM1246 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2885] VGAM1243 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1243 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1243 host target RNA into VGAM1243 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2886] VGAM1244 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1244 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1244 host target RNA into VGAM1244 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2887] VGAM1245 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1245 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1245 host target RNA into VGAM1245 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2888] VGAM1246 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1246 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1246 host target RNA into VGAM1246 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2889] It is appreciated that a function of VGR3011 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3011 gene include diagnosis, prevention and treatment of viral infection by Turkey Adenovirus 3. Specific functions, and accordingly utilities, of VGR3011 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3011 gene: VGAM1243 host target protein, VGAM1244 host target protein, VGAM1245 host target protein and VGAM1246 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1243, VGAM1244, VGAM1245 and VGAM1246. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3012(VGR3012) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2890] VGR3012 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3012 gene was detected is described hereinabove with reference to Figs. 1-9.

[2891] VGR3012 gene encodes VGR3012 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2892] VGR3012 precursor RNA folds spatially, forming VGR3012 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3012 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3012 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2893] VGR3012 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1247 precursor RNA, VGAM1248 precursor RNA, VGAM1249 precursor RNA, VGAM1250 precursor RNA and VGAM1251 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2894] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1247 RNA, VGAM1248 RNA, VGAM1249 RNA, VGAM1250 RNA and VGAM1251 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2895] VGAM1247 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1247 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1247 host target RNA into VGAM1247 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2896] VGAM1248 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1248 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1248 host target RNA into VGAM1248 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2897] VGAM1249 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1249 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1249 host target RNA into VGAM1249 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2898] VGAM1250 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1250 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1250 host target RNA into VGAM1250 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2899] VGAM1251 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1251 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1251 host target RNA into

VGAM1251 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2900] It is appreciated that a function of VGR3012 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3012 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3012 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3012 gene: VGAM1247 host target protein, VGAM1248 host target protein, VGAM1249 host target protein, VGAM1250 host target protein and VGAM1251 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1247, VGAM1248, VGAM1249, VGAM1250 and VGAM1251. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record

3013(VGR3013) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[2901] VGR3013 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3013 gene was
detected is described hereinabove with reference to Figs.
1-9.

[2902] VGR3013 gene encodes VGR3013 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[2903] VGR3013 precursor RNA folds spatially, forming VGR3013
folded precursor RNA, herein designated VGR FOLDED
PRECURSOR RNA. It is appreciated that VGR3013 folded
precursor RNA comprises a plurality of what is known in
the art as `hairpin` structures. These `hairpin` structures
are due to the fact that the nucleotide sequence of
VGR3013 precursor RNA comprises a plurality of seg-
ments, the first half of each such segment having a nu-
cleotide sequence which is at least a partial inversed-re-
versed sequence of the second half thereof, as is well

known in the art.

[2904] VGR3013 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1252 precursor RNA, VGAM1253 precursor RNA, VGAM1254 precursor RNA, VGAM1255 precursor RNA and VGAM1256 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2905] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1252 RNA, VGAM1253 RNA, VGAM1254 RNA, VGAM1255 RNA and VGAM1256 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2906] VGAM1252 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1252 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1252 host target RNA into VGAM1252 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2907] VGAM1253 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1253 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1253 host target RNA into VGAM1253 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2908] VGAM1254 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1254 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1254 host target RNA into VGAM1254 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2909] VGAM1255 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1255 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1255 host target RNA into VGAM1255 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2910] VGAM1256 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1256 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1256 host target RNA into VGAM1256 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2911] It is appreciated that a function of VGR3013 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3013 gene include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGR3013 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3013 gene: VGAM1252 host target protein, VGAM1253 host target protein, VGAM1254 host target protein, VGAM1255 host target protein and VGAM1256 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1252, VGAM1253, VGAM1254, VGAM1255 and VGAM1256. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3014(VGR3014) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2912] VGR3014 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3014 gene was detected is described hereinabove with reference to Figs. 1-9.

[2913] VGR3014 gene encodes VGR3014 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2914] VGR3014 precursor RNA folds spatially, forming VGR3014 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3014 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3014 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2915] VGR3014 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1257 precursor RNA and VGAM1258 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2916] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1257 RNA and VGAM1258 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2917] VGAM1257 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1257 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1257 host target RNA into VGAM1257 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2918] VGAM1258 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1258 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1258 host target RNA into VGAM1258 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2919] It is appreciated that a function of VGR3014 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3014 gene include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGR3014 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3014 gene: VGAM1257 host target protein and VGAM1258 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1257 and VGAM1258. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3015(VGR3015) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2920] VGR3015 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3015 gene was detected is described hereinabove with reference to Figs. 1-9.

[2921] VGR3015 gene encodes VGR3015 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2922] VGR3015 precursor RNA folds spatially, forming VGR3015 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3015 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3015 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2923] VGR3015 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1259 precursor RNA, VGAM1260 precursor RNA, VGAM1261 precursor RNA and VGAM1262 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2924] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1259 RNA, VGAM1260 RNA, VGAM1261 RNA and VGAM1262 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2925] VGAM1259 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1259 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1259 host target RNA into VGAM1259 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2926] VGAM1260 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1260 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1260 host target RNA into VGAM1260 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2927] VGAM1261 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1261 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1261 host target RNA into VGAM1261 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2928] VGAM1262 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1262 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1262 host target RNA into VGAM1262 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2929] It is appreciated that a function of VGR3015 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3015 gene include diagnosis, prevention and treatment of viral infection by Blackcurrant Reversion Virus. Specific functions, and accordingly utilities, of VGR3015 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3015 gene: VGAM1259

host target protein, VGAM1260 host target protein, VGAM1261 host target protein and VGAM1262 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1259, VGAM1260, VGAM1261 and VGAM1262. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3016(VGR3016) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2930] VGR3016 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3016 gene was detected is described hereinabove with reference to Figs. 1-9.

[2931] VGR3016 gene encodes VGR3016 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2932] VGR3016 precursor RNA folds spatially, forming VGR3016

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3016 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3016 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2933] VGR3016 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1263 precursor RNA, VGAM1264 precursor RNA, VGAM1265 precursor RNA, VGAM1266 precursor RNA and VGAM1267 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2934] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1263

RNA, VGAM1264 RNA, VGAM1265 RNA, VGAM1266 RNA and VGAM1267 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2935] VGAM1263 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1263 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1263 host target RNA into VGAM1263 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2936] VGAM1264 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1264 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1264 host target RNA into VGAM1264 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2937] VGAM1265 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1265 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1265 host target RNA into VGAM1265 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2938] VGAM1266 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1266 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1266 host target RNA into VGAM1266 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2939] VGAM1267 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1267 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1267 host target RNA into VGAM1267 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2940] It is appreciated that a function of VGR3016 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3016 gene include diagnosis, prevention and treatment of viral infection by

Beet Soil-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGR3016 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3016 gene: VGAM1263 host target protein, VGAM1264 host target protein, VGAM1265 host target protein, VGAM1266 host target protein and VGAM1267 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1263, VGAM1264, VGAM1265, VGAM1266 and VGAM1267. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3017(VGR3017) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2941] VGR3017 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3017 gene was

detected is described hereinabove with reference to Figs. 1-9.

[2942] VGR3017 gene encodes VGR3017 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2943] VGR3017 precursor RNA folds spatially, forming VGR3017 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3017 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3017 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2944] VGR3017 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1268 precursor RNA, VGAM1269 precursor RNA, VGAM1270 precursor RNA, VGAM1271 precursor RNA and VGAM1272 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2945] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1268 RNA, VGAM1269 RNA, VGAM1270 RNA, VGAM1271 RNA and VGAM1272 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2946] VGAM1268 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1268 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1268 host target RNA into VGAM1268 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2947] VGAM1269 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1269 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1269 host target RNA into VGAM1269 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2948] VGAM1270 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1270 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1270 host target RNA into VGAM1270 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2949] VGAM1271 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1271 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1271 host target RNA into VGAM1271 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2950] VGAM1272 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1272 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1272 host target RNA into VGAM1272 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2951] It is appreciated that a function of VGR3017 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3017 gene include diagnosis, prevention and treatment of viral infection by Grapevine Virus A. Specific functions, and accordingly utilities, of VGR3017 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3017 gene: VGAM1268 host target protein, VGAM1269 host target protein, VGAM1270 host target protein, VGAM1271 host target protein and VGAM1272 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1268, VGAM1269, VGAM1270, VGAM1271 and VGAM1272. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3018(VGR3018) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2952] VGR3018 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3018 gene was detected is described hereinabove with reference to Figs. 1-9.

[2953] VGR3018 gene encodes VGR3018 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2954] VGR3018 precursor RNA folds spatially, forming VGR3018 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3018 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3018 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2955] VGR3018 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1273 precursor RNA, VGAM1274 precursor RNA, VGAM1275 precursor RNA and VGAM1276 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2956] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1273 RNA, VGAM1274 RNA, VGAM1275 RNA and VGAM1276 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2957] VGAM1273 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1273 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1273 host target RNA into VGAM1273 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2958] VGAM1274 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1274 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1274 host target RNA into VGAM1274 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2959] VGAM1275 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1275 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1275 host target RNA into VGAM1275 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2960] VGAM1276 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1276 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1276 host target RNA into VGAM1276 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2961] It is appreciated that a function of VGR3018 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3018 gene include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific functions, and accordingly utili-

ties, of VGR3018 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3018 gene: VGAM1273 host target protein, VGAM1274 host target protein, VGAM1275 host target protein and VGAM1276 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1273, VGAM1274, VGAM1275 and VGAM1276. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3019(VGR3019) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2962] VGR3019 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3019 gene was detected is described hereinabove with reference to Figs. 1-9.

- [2963] VGR3019 gene encodes VGR3019 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [2964] VGR3019 precursor RNA folds spatially, forming VGR3019 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3019 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3019 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [2965] VGR3019 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1277 precursor RNA, VGAM1278 precursor RNA, VGAM1279 precursor RNA and VGAM1280 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2966] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1277 RNA, VGAM1278 RNA, VGAM1279 RNA and VGAM1280 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2967] VGAM1277 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1277 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1277 host target RNA into VGAM1277 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2968] VGAM1278 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1278 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1278 host target RNA into VGAM1278 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2969] VGAM1279 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1279 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1279 host target RNA into VGAM1279 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2970] VGAM1280 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1280 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1280 host target RNA into VGAM1280 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2971] It is appreciated that a function of VGR3019 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3019 gene include diagnosis, prevention and treatment of viral infection by Human Enterovirus C. Specific functions, and accordingly utilities, of VGR3019 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3019 gene: VGAM1277 host target protein, VGAM1278 host target protein, VGAM1279 host target protein and VGAM1280 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The

function of these host target genes is elaborated herein—above with reference to VGAM1277, VGAM1278, VGAM1279 and VGAM1280. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3020 (VGR3020) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2972] VGR3020 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3020 gene was detected is described hereinabove with reference to Figs. 1–9.

[2973] VGR3020 gene encodes VGR3020 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2974] VGR3020 precursor RNA folds spatially, forming VGR3020 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3020 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3020 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2975] VGR3020 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1281 precursor RNA, VGAM1282 precursor RNA, VGAM1283 precursor RNA, VGAM1284 precursor RNA, VGAM1285 precursor RNA, VGAM1286 precursor RNA and VGAM1287 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2976] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1281 RNA, VGAM1282 RNA, VGAM1283 RNA, VGAM1284 RNA, VGAM1285 RNA, VGAM1286 RNA and VGAM1287 RNA, herein schematically represented by VGAM1 RNA through

VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2977] VGAM1281 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1281 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1281 host target RNA into VGAM1281 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2978] VGAM1282 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1282 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1282 host target RNA into

VGAM1282 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2979] VGAM1283 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1283 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1283 host target RNA into VGAM1283 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2980] VGAM1284 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1284 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1284 host target RNA into VGAM1284 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2981] VGAM1285 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1285 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1285 host target RNA into VGAM1285 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2982] VGAM1286 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1286 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1286 host target RNA into VGAM1286 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2983] VGAM1287 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1287 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1287 host target RNA into VGAM1287 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2984] It is appreciated that a function of VGR3020 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3020 gene include diagnosis, prevention and treatment of viral infection by Beet Virus Q. Specific functions, and accordingly utilities,

of VGR3020 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3020 gene: VGAM1281 host target protein, VGAM1282 host target protein, VGAM1283 host target protein, VGAM1284 host target protein, VGAM1285 host target protein, VGAM1286 host target protein and VGAM1287 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1281, VGAM1282, VGAM1283, VGAM1284, VGAM1285, VGAM1286 and VGAM1287. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3021(VGR3021) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2985] VGR3021 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3021 gene was

detected is described hereinabove with reference to Figs. 1–9.

[2986] VGR3021 gene encodes VGR3021 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2987] VGR3021 precursor RNA folds spatially, forming VGR3021 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3021 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3021 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2988] VGR3021 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1288 precursor RNA and VGAM1289 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to

VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [2989] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1288 RNA and VGAM1289 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [2990] VGAM1288 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1288 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1288 host target RNA into VGAM1288 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [2991] VGAM1289 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1289 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1289 host target RNA into VGAM1289 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2992] It is appreciated that a function of VGR3021 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3021 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3021 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3021 gene: VGAM1288 host target protein and VGAM1289 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1288 and VGAM1289. Fig. 9 fur-

ther provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3022(VGR3022) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[2993] VGR3022 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3022 gene was detected is described hereinabove with reference to Figs. 1-9.

[2994] VGR3022 gene encodes VGR3022 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[2995] VGR3022 precursor RNA folds spatially, forming VGR3022 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3022 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3022 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[2996] VGR3022 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1291 precursor RNA, VGAM1292 precursor RNA and VGAM1293 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[2997] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1291 RNA, VGAM1292 RNA and VGAM1293 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[2998] VGAM1291 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1291 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1291 host target RNA into VGAM1291 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[2999] VGAM1292 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1292 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1292 host target RNA into VGAM1292 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3000] VGAM1293 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1293 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1293 host target RNA into VGAM1293 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3001] It is appreciated that a function of VGR3022 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3022 gene include diagnosis, prevention and treatment of viral infection by Swinepox Virus. Specific functions, and accordingly utilities, of VGR3022 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3022 gene: VGAM1291 host target protein, VGAM1292 host target protein and VGAM1293 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1291, VGAM1292 and VGAM1293. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3023(VGR3023) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3002] VGR3023 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3023 gene was detected is described hereinabove with reference to Figs. 1-9.

[3003] VGR3023 gene encodes VGR3023 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3004] VGR3023 precursor RNA folds spatially, forming VGR3023 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3023 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3023 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3005] VGR3023 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1294 precursor RNA, VGAM1295 precursor RNA and VGAM1296 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3006] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1294 RNA, VGAM1295 RNA and VGAM1296 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3007] VGAM1294 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1294 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1294 host target RNA into VGAM1294 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3008] VGAM1295 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1295 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1295 host target RNA into VGAM1295 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3009] VGAM1296 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1296 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1296 host target RNA into VGAM1296 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3010] It is appreciated that a function of VGR3023 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3023 gene include diagnosis, prevention and treatment of viral infection by Vaccinia Virus. Specific functions, and accordingly utilities, of VGR3023 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3023 gene: VGAM1294 host target protein,

VGAM1295 host target protein and VGAM1296 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1294, VGAM1295 and VGAM1296. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3024(VGR3024) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3011] VGR3024 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3024 gene was detected is described hereinabove with reference to Figs. 1-9.

[3012] VGR3024 gene encodes VGR3024 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3013] VGR3024 precursor RNA folds spatially, forming VGR3024 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3024 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3024 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3014] VGR3024 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1297 precursor RNA, VGAM1298 precursor RNA, VGAM1299 precursor RNA, VGAM1300 precursor RNA and VGAM1301 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3015] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1297 RNA, VGAM1298 RNA, VGAM1299 RNA, VGAM1300 RNA

and VGAM1301 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3016] VGAM1297 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1297 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1297 host target RNA into VGAM1297 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3017] VGAM1298 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1298 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1298 host target RNA into VGAM1298 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3018] VGAM1299 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1299 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1299 host target RNA into VGAM1299 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3019] VGAM1300 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1300 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1300 host target RNA into VGAM1300 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3020] VGAM1301 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1301 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1301 host target RNA into VGAM1301 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3021] It is appreciated that a function of VGR3024 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3024 gene include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accord-

ingly utilities, of VGR3024 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3024 gene: VGAM1297 host target protein, VGAM1298 host target protein, VGAM1299 host target protein, VGAM1300 host target protein and VGAM1301 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1297, VGAM1298, VGAM1299, VGAM1300 and VGAM1301. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3025(VGR3025) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3022] VGR3025 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3025 gene was detected is described hereinabove with reference to Figs.

1-9.

[3023] VGR3025 gene encodes VGR3025 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3024] VGR3025 precursor RNA folds spatially, forming VGR3025 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3025 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3025 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3025] VGR3025 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1302 precursor RNA, VGAM1303 precursor RNA and VGAM1304 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[3026] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1302 RNA, VGAM1303 RNA and VGAM1304 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3027] VGAM1302 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1302 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1302 host target RNA into VGAM1302 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3028] VGAM1303 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1303 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1303 host target RNA into VGAM1303 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3029] VGAM1304 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1304 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1304 host target RNA into VGAM1304 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3030] It is appreciated that a function of VGR3025 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3025 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGR3025 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3025 gene: VGAM1302 host target protein, VGAM1303 host target protein and VGAM1304 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1302, VGAM1303 and VGAM1304. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3026(VGR3026) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3031] VGR3026 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3026 gene was detected is described hereinabove with reference to Figs. 1-9.

[3032] VGR3026 gene encodes VGR3026 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3033] VGR3026 precursor RNA folds spatially, forming VGR3026 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3026 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3026 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3034] VGR3026 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1305 precursor RNA, VGAM1306 precursor RNA, VGAM1307 precursor RNA and VGAM1308 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3035] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1305 RNA, VGAM1306 RNA, VGAM1307 RNA and VGAM1308 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3036] VGAM1305 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1305 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1305 host target RNA into VGAM1305 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3037] VGAM1306 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1306 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1306 host target RNA into VGAM1306 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3038] VGAM1307 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1307 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1307 host target RNA into VGAM1307 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3039] VGAM1308 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1308 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1308 host target RNA into VGAM1308 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3040] It is appreciated that a function of VGR3026 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3026 gene include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus SAT 2 (FMDV-SAT2). Specific functions, and accordingly utilities, of VGR3026 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3026 gene:

VGAM1305 host target protein, VGAM1306 host target protein, VGAM1307 host target protein and VGAM1308 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1305, VGAM1306, VGAM1307 and VGAM1308. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3027 (VGR3027) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3041] VGR3027 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3027 gene was detected is described hereinabove with reference to Figs. 1-9.

[3042] VGR3027 gene encodes VGR3027 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3043] VGR3027 precursor RNA folds spatially, forming VGR3027

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3027 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3027 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3044] VGR3027 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1309 precursor RNA and VGAM1310 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3045] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1309 RNA and VGAM1310 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3046] VGAM1309 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1309 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1309 host target RNA into VGAM1309 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3047] VGAM1310 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1310 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1310 host target RNA into VGAM1310 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3048] It is appreciated that a function of VGR3027 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3027 gene include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGR3027 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3027 gene: VGAM1309 host target protein and VGAM1310 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1309 and VGAM1310. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3028(VGR3028) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[3049] VGR3028 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3028 gene was detected is described hereinabove with reference to Figs. 1-9.

[3050] VGR3028 gene encodes VGR3028 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3051] VGR3028 precursor RNA folds spatially, forming VGR3028 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3028 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3028 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3052] VGR3028 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM

precursor RNAs, VGAM1311 precursor RNA, VGAM1312 precursor RNA, VGAM1313 precursor RNA, VGAM1314 precursor RNA, VGAM1315 precursor RNA and VGAM1316 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3053] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1311 RNA, VGAM1312 RNA, VGAM1313 RNA, VGAM1314 RNA, VGAM1315 RNA and VGAM1316 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3054] VGAM1311 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1311 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1311 host target RNA into VGAM1311 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3055] VGAM1312 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1312 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1312 host target RNA into VGAM1312 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3056] VGAM1313 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1313 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1313 host target RNA into VGAM1313 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3057] VGAM1314 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1314 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1314 host target RNA into VGAM1314 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3058] VGAM1315 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1315 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1315 host target RNA into VGAM1315 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3059] VGAM1316 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1316 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1316 host target RNA into VGAM1316 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3060] It is appreciated that a function of VGR3028 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3028 gene include

diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus C. Specific functions, and accordingly utilities, of VGR3028 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3028 gene: VGAM1311 host target protein, VGAM1312 host target protein, VGAM1313 host target protein, VGAM1314 host target protein, VGAM1315 host target protein and VGAM1316 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1311, VGAM1312, VGAM1313, VGAM1314, VGAM1315 and VGAM1316. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3029(VGR3029) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3061] VGR3029 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3029 gene was detected is described hereinabove with reference to Figs. 1-9.

[3062] VGR3029 gene encodes VGR3029 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3063] VGR3029 precursor RNA folds spatially, forming VGR3029 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3029 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3029 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3064] VGR3029 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1317 precursor RNA, VGAM1318 precursor RNA and VGAM1319 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3065] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1317 RNA, VGAM1318 RNA and VGAM1319 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3066] VGAM1317 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1317 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1317 host target RNA into VGAM1317 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3067] VGAM1318 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1318 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1318 host target RNA into VGAM1318 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3068] VGAM1319 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1319 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1319 host target RNA into VGAM1319 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3069] It is appreciated that a function of VGR3029 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3029 gene include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus O. Specific functions, and accordingly utilities, of VGR3029 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3029 gene: VGAM1317 host target protein, VGAM1318 host target protein and VGAM1319 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1317, VGAM1318 and VGAM1319. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3030(VGR3030) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[3070] VGR3030 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3030 gene was detected is described hereinabove with reference to Figs. 1-9.

[3071] VGR3030 gene encodes VGR3030 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3072] VGR3030 precursor RNA folds spatially, forming VGR3030 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3030 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3030 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3073] VGR3030 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1320 precursor RNA and VGAM1321 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3074] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1320 RNA and VGAM1321 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3075] VGAM1320 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1320 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1320 host target RNA into

VGAM1320 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3076] VGAM1321 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1321 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1321 host target RNA into VGAM1321 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3077] It is appreciated that a function of VGR3030 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3030 gene include diagnosis, prevention and treatment of viral infection by Melanoplus Sanguinipes Entomopoxvirus. Specific functions, and accordingly utilities, of VGR3030 gene correlate with, and may be deduced from, the identity of the host

target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3030 gene: VGAM1320 host target protein and VGAM1321 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1320 and VGAM1321. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3031(VGR3031) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3078] VGR3031 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3031 gene was detected is described hereinabove with reference to Figs. 1-9.

[3079] VGR3031 gene encodes VGR3031 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3080] VGR3031 precursor RNA folds spatially, forming VGR3031 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3031 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3031 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3081] VGR3031 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1322 precursor RNA, VGAM1323 precursor RNA, VGAM1324 precursor RNA and VGAM1325 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3082] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1322

RNA, VGAM1323 RNA, VGAM1324 RNA and VGAM1325 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3083] VGAM1322 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1322 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1322 host target RNA into VGAM1322 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3084] VGAM1323 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1323 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1323 host target RNA into VGAM1323 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3085] VGAM1324 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1324 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1324 host target RNA into VGAM1324 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3086] VGAM1325 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1325 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1325 host target RNA into VGAM1325 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3087] It is appreciated that a function of VGR3031 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3031 gene include diagnosis, prevention and treatment of viral infection by Garlic Latent Virus. Specific functions, and accordingly utilities, of VGR3031 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3031 gene: VGAM1322 host target protein, VGAM1323 host target protein, VGAM1324 host target protein and VGAM1325 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1322, VGAM1323, VGAM1324 and VGAM1325. Fig. 9 further provides a con-

ceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3032(VGR3032) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3088] VGR3032 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3032 gene was detected is described hereinabove with reference to Figs. 1-9.

[3089] VGR3032 gene encodes VGR3032 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3090] VGR3032 precursor RNA folds spatially, forming VGR3032 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3032 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3032 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3091] VGR3032 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1326 precursor RNA, VGAM1327 precursor RNA and VGAM1328 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3092] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1326 RNA, VGAM1327 RNA and VGAM1328 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3093] VGAM1326 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1326 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1326 host target RNA into VGAM1326 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3094] VGAM1327 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1327 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1327 host target RNA into VGAM1327 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3095] VGAM1328 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1328 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1328 host target RNA into VGAM1328 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3096] It is appreciated that a function of VGR3032 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3032 gene include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGR3032 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3032 gene: VGAM1326 host target protein, VGAM1327 host target protein and VGAM1328 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these

host target genes is elaborated hereinabove with reference to VGAM1326, VGAM1327 and VGAM1328. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3033(VGR3033) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3097] VGR3033 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3033 gene was detected is described hereinabove with reference to Figs. 1-9.

[3098] VGR3033 gene encodes VGR3033 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3099] VGR3033 precursor RNA folds spatially, forming VGR3033 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3033 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3033 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3100] VGR3033 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1330 precursor RNA, VGAM1331 precursor RNA, VGAM1332 precursor RNA, VGAM1333 precursor RNA, VGAM1334 precursor RNA and VGAM1335 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3101] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1330 RNA, VGAM1331 RNA, VGAM1332 RNA, VGAM1333 RNA, VGAM1334 RNA and VGAM1335 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of

Fig. 1.

[3102] VGAM1330 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1330 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1330 host target RNA into VGAM1330 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3103] VGAM1331 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1331 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1331 host target RNA into VGAM1331 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3104] VGAM1332 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1332 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1332 host target RNA into VGAM1332 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3105] VGAM1333 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1333 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1333 host target RNA into

VGAM1333 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3106] VGAM1334 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1334 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1334 host target RNA into VGAM1334 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3107] VGAM1335 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1335 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1335 host target RNA into VGAM1335 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3108] It is appreciated that a function of VGR3033 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3033 gene include diagnosis, prevention and treatment of viral infection by Human Adenovirus A. Specific functions, and accordingly utilities, of VGR3033 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3033 gene: VGAM1330 host target protein, VGAM1331 host target protein, VGAM1332 host target protein, VGAM1333 host target protein, VGAM1334 host target protein and VGAM1335 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1330, VGAM1331, VGAM1332, VGAM1333, VGAM1334 and VGAM1335. Fig. 9 further provides a conceptual description of novel

bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3034(VGR3034) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3109] VGR3034 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3034 gene was detected is described hereinabove with reference to Figs. 1-9.

[3110] VGR3034 gene encodes VGR3034 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3111] VGR3034 precursor RNA folds spatially, forming VGR3034 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3034 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3034 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3112] VGR3034 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1336 precursor RNA and VGAM1337 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3113] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1336 RNA and VGAM1337 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3114] VGAM1336 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1336 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1336 host target RNA into VGAM1336 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3115] VGAM1337 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1337 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1337 host target RNA into VGAM1337 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3116] It is appreciated that a function of VGR3034 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3034 gene include diagnosis, prevention and treatment of viral infection by

Sheeppox Virus. Specific functions, and accordingly utilities, of VGR3034 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3034 gene: VGAM1336 host target protein and VGAM1337 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1336 and VGAM1337. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3035(VGR3035) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3117] VGR3035 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3035 gene was detected is described hereinabove with reference to Figs. 1-9.

- [3118] VGR3035 gene encodes VGR3035 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [3119] VGR3035 precursor RNA folds spatially, forming VGR3035 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3035 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3035 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [3120] VGR3035 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1340 precursor RNA, VGAM1341 precursor RNA, VGAM1342 precursor RNA and VGAM1343 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [3121] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1340 RNA, VGAM1341 RNA, VGAM1342 RNA and VGAM1343 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [3122] VGAM1340 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1340 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1340 host target RNA into VGAM1340 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [3123] VGAM1341 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1341 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1341 host target RNA into VGAM1341 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3124] VGAM1342 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1342 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1342 host target RNA into VGAM1342 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3125] VGAM1343 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1343 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1343 host target RNA into VGAM1343 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3126] It is appreciated that a function of VGR3035 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3035 gene include diagnosis, prevention and treatment of viral infection by Garlic Virus A. Specific functions, and accordingly utilities, of VGR3035 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3035 gene: VGAM1340 host target protein, VGAM1341 host target protein, VGAM1342 host target protein and VGAM1343 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM1340, VGAM1341, VGAM1342 and VGAM1343. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3036(VGR3036) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3127] VGR3036 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3036 gene was detected is described hereinabove with reference to Figs. 1-9.

[3128] VGR3036 gene encodes VGR3036 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3129] VGR3036 precursor RNA folds spatially, forming VGR3036 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3036 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3036 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3130] VGR3036 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1346 precursor RNA, VGAM1347 precursor RNA, VGAM1348 precursor RNA, VGAM1349 precursor RNA, VGAM1350 precursor RNA, VGAM1351 precursor RNA, VGAM1352 precursor RNA and VGAM1353 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3131] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1346 RNA, VGAM1347 RNA, VGAM1348 RNA, VGAM1349 RNA, VGAM1350 RNA, VGAM1351 RNA, VGAM1352 RNA and VGAM1353 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3132] VGAM1346 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1346 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1346 host target RNA into VGAM1346 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3133] VGAM1347 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1347 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1347 host target RNA into

VGAM1347 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3134] VGAM1348 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1348 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1348 host target RNA into VGAM1348 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3135] VGAM1349 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1349 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1349 host target RNA into VGAM1349 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3136] VGAM1350 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1350 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1350 host target RNA into VGAM1350 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3137] VGAM1351 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1351 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1351 host target RNA into VGAM1351 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3138] VGAM1352 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1352 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1352 host target RNA into VGAM1352 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3139] VGAM1353 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1353 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1353 host target RNA into VGAM1353 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3140] It is appreciated that a function of VGR3036 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3036 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3036 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3036 gene: VGAM1346 host target protein, VGAM1347 host target protein, VGAM1348 host target protein, VGAM1349 host target protein, VGAM1350 host target protein, VGAM1351 host target protein, VGAM1352 host target protein and VGAM1353 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes

is elaborated hereinabove with reference to VGAM1346, VGAM1347, VGAM1348, VGAM1349, VGAM1350, VGAM1351, VGAM1352 and VGAM1353. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3037 (VGR3037) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3141] VGR3037 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3037 gene was detected is described hereinabove with reference to Figs. 1-9.

[3142] VGR3037 gene encodes VGR3037 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3143] VGR3037 precursor RNA folds spatially, forming VGR3037 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3037 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3037 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3144] VGR3037 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1354 precursor RNA, VGAM1355 precursor RNA, VGAM1356 precursor RNA, VGAM1357 precursor RNA, VGAM1358 precursor RNA, VGAM1359 precursor RNA, VGAM1360 precursor RNA and VGAM1361 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3145] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1354 RNA, VGAM1355 RNA, VGAM1356 RNA, VGAM1357 RNA, VGAM1358 RNA, VGAM1359 RNA, VGAM1360 RNA and VGAM1361 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3146] VGAM1354 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1354 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1354 host target RNA into VGAM1354 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3147] VGAM1355 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1355 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1355 host target RNA into

VGAM1355 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3148] VGAM1356 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1356 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1356 host target RNA into VGAM1356 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3149] VGAM1357 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1357 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1357 host target RNA into VGAM1357 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3150] VGAM1358 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1358 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1358 host target RNA into VGAM1358 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3151] VGAM1359 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1359 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1359 host target RNA into VGAM1359 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3152] VGAM1360 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1360 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1360 host target RNA into VGAM1360 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3153] VGAM1361 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1361 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1361 host target RNA into VGAM1361 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3154] It is appreciated that a function of VGR3037 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3037 gene include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGR3037 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3037 gene: VGAM1354 host target protein, VGAM1355 host target protein, VGAM1356 host target protein, VGAM1357 host target protein, VGAM1358 host target protein, VGAM1359 host target protein, VGAM1360 host target protein and VGAM1361 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes

is elaborated hereinabove with reference to VGAM1354, VGAM1355, VGAM1356, VGAM1357, VGAM1358, VGAM1359, VGAM1360 and VGAM1361. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3038 (VGR3038) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3155] VGR3038 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3038 gene was detected is described hereinabove with reference to Figs. 1-9.

[3156] VGR3038 gene encodes VGR3038 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3157] VGR3038 precursor RNA folds spatially, forming VGR3038 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3038 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3038 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3158] VGR3038 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1362 precursor RNA, VGAM1363 precursor RNA, VGAM1364 precursor RNA and VGAM1365 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3159] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1362 RNA, VGAM1363 RNA, VGAM1364 RNA and VGAM1365 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3160] VGAM1362 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1362 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1362 host target RNA into VGAM1362 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3161] VGAM1363 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1363 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1363 host target RNA into VGAM1363 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3162] VGAM1364 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1364 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1364 host target RNA into VGAM1364 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3163] VGAM1365 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1365 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1365 host target RNA into VGAM1365 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3164] It is appreciated that a function of VGR3038 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3038 gene include diagnosis, prevention and treatment of viral infection by Duck Adenovirus 1. Specific functions, and accordingly utilities, of VGR3038 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3038 gene: VGAM1362 host target protein, VGAM1363 host target protein, VGAM1364 host target protein and VGAM1365 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1362, VGAM1363, VGAM1364 and VGAM1365. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3039(VGR3039) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[3165] VGR3039 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3039 gene was detected is described hereinabove with reference to Figs. 1-9.

[3166] VGR3039 gene encodes VGR3039 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3167] VGR3039 precursor RNA folds spatially, forming VGR3039 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3039 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3039 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3168] VGR3039 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM

precursor RNAs, VGAM1366 precursor RNA, VGAM1367 precursor RNA, VGAM1368 precursor RNA, VGAM1369 precursor RNA, VGAM1370 precursor RNA and VGAM1371 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3169] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1366 RNA, VGAM1367 RNA, VGAM1368 RNA, VGAM1369 RNA, VGAM1370 RNA and VGAM1371 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3170] VGAM1366 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1366 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1366 host target RNA into VGAM1366 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3171] VGAM1367 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1367 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1367 host target RNA into VGAM1367 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3172] VGAM1368 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1368 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1368 host target RNA into VGAM1368 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3173] VGAM1369 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1369 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1369 host target RNA into VGAM1369 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3174] VGAM1370 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1370 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1370 host target RNA into VGAM1370 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3175] VGAM1371 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1371 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1371 host target RNA into VGAM1371 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3176] It is appreciated that a function of VGR3039 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3039 gene include

diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGR3039 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3039 gene: VGAM1366 host target protein, VGAM1367 host target protein, VGAM1368 host target protein, VGAM1369 host target protein, VGAM1370 host target protein and VGAM1371 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1366, VGAM1367, VGAM1368, VGAM1369, VGAM1370 and VGAM1371. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3040(VGR3040) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3177] VGR3040 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3040 gene was detected is described hereinabove with reference to Figs. 1-9.

[3178] VGR3040 gene encodes VGR3040 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3179] VGR3040 precursor RNA folds spatially, forming VGR3040 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3040 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3040 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3180] VGR3040 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1372 precursor RNA, VGAM1373 precursor RNA, VGAM1374 precursor RNA, VGAM1375 precursor RNA, VGAM1376 precursor RNA and VGAM1377

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3181] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1372 RNA, VGAM1373 RNA, VGAM1374 RNA, VGAM1375 RNA, VGAM1376 RNA and VGAM1377 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3182] VGAM1372 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1372 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1372 host target RNA into VGAM1372 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3183] VGAM1373 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1373 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1373 host target RNA into VGAM1373 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3184] VGAM1374 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1374 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1374 host target RNA into

VGAM1374 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3185] VGAM1375 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1375 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1375 host target RNA into VGAM1375 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3186] VGAM1376 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1376 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1376 host target RNA into VGAM1376 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3187] VGAM1377 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1377 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1377 host target RNA into VGAM1377 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3188] It is appreciated that a function of VGR3040 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3040 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3040 gene correlate with, and may

be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3040 gene: VGAM1372 host target protein, VGAM1373 host target protein, VGAM1374 host target protein, VGAM1375 host target protein, VGAM1376 host target protein and VGAM1377 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1372, VGAM1373, VGAM1374, VGAM1375, VGAM1376 and VGAM1377. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3041(VGR3041) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3189] VGR3041 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3041 gene was detected is described hereinabove with reference to Figs.

1-9.

[3190] VGR3041 gene encodes VGR3041 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3191] VGR3041 precursor RNA folds spatially, forming VGR3041 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3041 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3041 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3192] VGR3041 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1378 precursor RNA and VGAM1379 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3193] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1378 RNA and VGAM1379 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3194] VGAM1378 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1378 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1378 host target RNA into VGAM1378 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3195] VGAM1379 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1379 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1379 host target RNA into VGAM1379 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3196] It is appreciated that a function of VGR3041 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3041 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3041 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3041 gene: VGAM1378 host target protein and VGAM1379 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1378 and VGAM1379. Fig. 9 further provides a conceptual description of novel bioinfor-

matically detected regulatory viral gene, referred to here as Viral Genomic Record 3042(VGR3042) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3197] VGR3042 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3042 gene was detected is described hereinabove with reference to Figs. 1-9.

[3198] VGR3042 gene encodes VGR3042 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3199] VGR3042 precursor RNA folds spatially, forming VGR3042 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3042 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3042 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3200] VGR3042 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1380 precursor RNA, VGAM1381 precursor RNA, VGAM1382 precursor RNA, VGAM1383 precursor RNA, VGAM1384 precursor RNA, VGAM1385 precursor RNA, VGAM1386 precursor RNA and VGAM1387 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3201] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1380 RNA, VGAM1381 RNA, VGAM1382 RNA, VGAM1383 RNA, VGAM1384 RNA, VGAM1385 RNA, VGAM1386 RNA and VGAM1387 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3202] VGAM1380 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1380 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1380 host target RNA into VGAM1380 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3203] VGAM1381 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1381 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1381 host target RNA into VGAM1381 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3204] VGAM1382 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1382 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1382 host target RNA into VGAM1382 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3205] VGAM1383 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1383 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1383 host target RNA into VGAM1383 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3206] VGAM1384 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1384 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1384 host target RNA into VGAM1384 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3207] VGAM1385 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1385 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1385 host target RNA into VGAM1385 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3208] VGAM1386 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1386 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1386 host target RNA into VGAM1386 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3209] VGAM1387 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1387 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1387 host target RNA into

VGAM1387 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3210] It is appreciated that a function of VGR3042 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3042 gene include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGR3042 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3042 gene: VGAM1380 host target protein, VGAM1381 host target protein, VGAM1382 host target protein, VGAM1383 host target protein, VGAM1384 host target protein, VGAM1385 host target protein, VGAM1386 host target protein and VGAM1387 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1380, VGAM1381, VGAM1382, VGAM1383, VGAM1384, VGAM1385, VGAM1386 and VGAM1387. Fig. 9 further

provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3043(VGR3043) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3211] VGR3043 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3043 gene was detected is described hereinabove with reference to Figs. 1-9.

[3212] VGR3043 gene encodes VGR3043 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3213] VGR3043 precursor RNA folds spatially, forming VGR3043 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3043 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3043 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3214] VGR3043 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1388 precursor RNA, VGAM1389 precursor RNA and VGAM1390 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3215] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1388 RNA, VGAM1389 RNA and VGAM1390 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3216] VGAM1388 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1388 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1388 host target RNA into VGAM1388 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3217] VGAM1389 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1389 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1389 host target RNA into VGAM1389 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3218] VGAM1390 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1390 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1390 host target RNA into VGAM1390 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3219] It is appreciated that a function of VGR3043 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3043 gene include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR3043 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3043 gene: VGAM1388 host target protein, VGAM1389 host target protein and VGAM1390 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these

host target genes is elaborated hereinabove with reference to VGAM1388, VGAM1389 and VGAM1390. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3044(VGR3044) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3220] VGR3044 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3044 gene was detected is described hereinabove with reference to Figs. 1-9.

[3221] VGR3044 gene encodes VGR3044 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3222] VGR3044 precursor RNA folds spatially, forming VGR3044 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3044 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3044 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3223] VGR3044 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1391 precursor RNA, VGAM1392 precursor RNA, VGAM1393 precursor RNA and VGAM1394 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3224] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1391 RNA, VGAM1392 RNA, VGAM1393 RNA and VGAM1394 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3225] VGAM1391 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1391 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1391 host target RNA into VGAM1391 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3226] VGAM1392 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1392 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1392 host target RNA into VGAM1392 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3227] VGAM1393 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1393 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1393 host target RNA into VGAM1393 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3228] VGAM1394 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1394 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1394 host target RNA into VGAM1394 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3229] It is appreciated that a function of VGR3044 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3044 gene include diagnosis, prevention and treatment of viral infection by Wheat Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGR3044 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3044 gene: VGAM1391 host target protein, VGAM1392 host target protein, VGAM1393 host target protein and VGAM1394 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1391, VGAM1392, VGAM1393 and VGAM1394. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3045(VGR3045) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[3230] VGR3045 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3045 gene was detected is described hereinabove with reference to Figs. 1-9.

[3231] VGR3045 gene encodes VGR3045 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3232] VGR3045 precursor RNA folds spatially, forming VGR3045 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3045 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3045 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3233] VGR3045 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM1395 precursor RNA, VGAM1396 precursor RNA and VGAM1397 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3234] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1395 RNA, VGAM1396 RNA and VGAM1397 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3235] VGAM1395 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1395 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1395 host target RNA into

VGAM1395 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3236] VGAM1396 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1396 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1396 host target RNA into VGAM1396 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3237] VGAM1397 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1397 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1397 host target RNA into VGAM1397 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3238] It is appreciated that a function of VGR3045 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3045 gene include diagnosis, prevention and treatment of viral infection by Cowpea Aphid-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGR3045 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3045 gene: VGAM1395 host target protein, VGAM1396 host target protein and VGAM1397 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1395, VGAM1396 and VGAM1397. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3046(VGR3046) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3239] VGR3046 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3046 gene was detected is described hereinabove with reference to Figs. 1-9.

[3240] VGR3046 gene encodes VGR3046 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3241] VGR3046 precursor RNA folds spatially, forming VGR3046 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3046 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3046 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[3242] VGR3046 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1398 precursor RNA, VGAM1399 precursor RNA, VGAM1400 precursor RNA, VGAM1401 precursor RNA, VGAM1402 precursor RNA, VGAM1403 precursor RNA and VGAM1404 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3243] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1398 RNA, VGAM1399 RNA, VGAM1400 RNA, VGAM1401 RNA, VGAM1402 RNA, VGAM1403 RNA and VGAM1404 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3244] VGAM1398 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1398 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1398 host target RNA into VGAM1398 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3245] VGAM1399 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1399 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1399 host target RNA into VGAM1399 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3246] VGAM1400 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1400 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1400 host target RNA into VGAM1400 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3247] VGAM1401 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1401 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1401 host target RNA into VGAM1401 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3248] VGAM1402 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1402 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1402 host target RNA into VGAM1402 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3249] VGAM1403 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1403 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1403 host target RNA into VGAM1403 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3250] VGAM1404 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1404 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1404 host target RNA into VGAM1404 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3251] It is appreciated that a function of VGR3046 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3046 gene include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGR3046 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3046 gene: VGAM1398 host target protein, VGAM1399 host target protein,

VGAM1400 host target protein, VGAM1401 host target protein, VGAM1402 host target protein, VGAM1403 host target protein and VGAM1404 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1398, VGAM1399, VGAM1400, VGAM1401, VGAM1402, VGAM1403 and VGAM1404. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3047(VGR3047) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3252] VGR3047 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3047 gene was detected is described hereinabove with reference to Figs. 1-9.

[3253] VGR3047 gene encodes VGR3047 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[3254] VGR3047 precursor RNA folds spatially, forming VGR3047 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3047 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3047 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3255] VGR3047 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1405 precursor RNA and VGAM1406 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3256] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1405

RNA and VGAM1406 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3257] VGAM1405 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1405 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1405 host target RNA into VGAM1405 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3258] VGAM1406 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1406 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1406 host target RNA into VGAM1406 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3259] It is appreciated that a function of VGR3047 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3047 gene include diagnosis, prevention and treatment of viral infection by Perina Nuda Picorna-like Virus. Specific functions, and accordingly utilities, of VGR3047 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3047 gene: VGAM1405 host target protein and VGAM1406 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1405 and VGAM1406. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3048(VGR3048) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3260] VGR3048 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3048 gene was detected is described hereinabove with reference to Figs. 1-9.

[3261] VGR3048 gene encodes VGR3048 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3262] VGR3048 precursor RNA folds spatially, forming VGR3048 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3048 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3048 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3263] VGR3048 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1407 precursor RNA, VGAM1408 precursor RNA, VGAM1409 precursor RNA, VGAM1410 precursor RNA and VGAM1411 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3264] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1407 RNA, VGAM1408 RNA, VGAM1409 RNA, VGAM1410 RNA and VGAM1411 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3265] VGAM1407 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1407 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1407 host target RNA into VGAM1407 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3266] VGAM1408 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1408 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1408 host target RNA into VGAM1408 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3267] VGAM1409 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1409 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1409 host target RNA into VGAM1409 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3268] VGAM1410 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1410 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1410 host target RNA into VGAM1410 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3269] VGAM1411 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1411 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1411 host target RNA into VGAM1411 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3270] It is appreciated that a function of VGR3048 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3048 gene include diagnosis, prevention and treatment of viral infection by Acute Bee Paralysis Virus. Specific functions, and accordingly utilities, of VGR3048 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3048 gene: VGAM1407 host target protein, VGAM1408 host target protein, VGAM1409 host target protein, VGAM1410 host target protein and VGAM1411 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these

host target genes is elaborated hereinabove with reference to VGAM1407, VGAM1408, VGAM1409, VGAM1410 and VGAM1411. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3049(VGR3049) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3271] VGR3049 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3049 gene was detected is described hereinabove with reference to Figs. 1-9.

[3272] VGR3049 gene encodes VGR3049 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3273] VGR3049 precursor RNA folds spatially, forming VGR3049 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3049 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3049 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3274] VGR3049 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1412 precursor RNA, VGAM1413 precursor RNA, VGAM1414 precursor RNA and VGAM1415 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3275] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1412 RNA, VGAM1413 RNA, VGAM1414 RNA and VGAM1415 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3276] VGAM1412 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1412 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1412 host target RNA into VGAM1412 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3277] VGAM1413 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1413 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1413 host target RNA into VGAM1413 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3278] VGAM1414 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1414 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1414 host target RNA into VGAM1414 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3279] VGAM1415 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1415 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1415 host target RNA into VGAM1415 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3280] It is appreciated that a function of VGR3049 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3049 gene include diagnosis, prevention and treatment of viral infection by Bean Yellow Mosaic Virus. Specific functions, and accordingly utilities, of VGR3049 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3049 gene: VGAM1412 host target protein, VGAM1413 host target protein, VGAM1414 host target protein and VGAM1415 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1412, VGAM1413, VGAM1414 and VGAM1415. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3050(VGR3050) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[3281] VGR3050 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3050 gene was detected is described hereinabove with reference to Figs. 1-9.

[3282] VGR3050 gene encodes VGR3050 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3283] VGR3050 precursor RNA folds spatially, forming VGR3050 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3050 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3050 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3284] VGR3050 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM

precursor RNAs, VGAM1416 precursor RNA, VGAM1417 precursor RNA, VGAM1418 precursor RNA and VGAM1419 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3285] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1416 RNA, VGAM1417 RNA, VGAM1418 RNA and VGAM1419 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3286] VGAM1416 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1416 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1416 host target RNA into

VGAM1416 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3287] VGAM1417 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1417 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1417 host target RNA into VGAM1417 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3288] VGAM1418 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1418 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1418 host target RNA into VGAM1418 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3289] VGAM1419 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1419 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1419 host target RNA into VGAM1419 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3290] It is appreciated that a function of VGR3050 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3050 gene include diagnosis, prevention and treatment of viral infection by Ryegrass Mosaic Virus. Specific functions, and accordingly utilities, of VGR3050 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3050 gene: VGAM1416 host target protein, VGAM1417 host target protein, VGAM1418 host target protein and VGAM1419 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1416, VGAM1417, VGAM1418 and VGAM1419. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3051(VGR3051) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3291] VGR3051 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3051 gene was detected is described hereinabove with reference to Figs. 1-9.

[3292] VGR3051 gene encodes VGR3051 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3293] VGR3051 precursor RNA folds spatially, forming VGR3051 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3051 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3051 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3294] VGR3051 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1420 precursor RNA, VGAM1421 precursor RNA, VGAM1422 precursor RNA and VGAM1423 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3295] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1420 RNA, VGAM1421 RNA, VGAM1422 RNA and VGAM1423 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3296] VGAM1420 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1420 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1420 host target RNA into VGAM1420 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3297] VGAM1421 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1421 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1421 host target RNA into VGAM1421 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3298] VGAM1422 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1422 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1422 host target RNA into VGAM1422 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3299] VGAM1423 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1423 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1423 host target RNA into VGAM1423 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3300] It is appreciated that a function of VGR3051 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3051 gene include diagnosis, prevention and treatment of viral infection by Hepatitis GB Virus A. Specific functions, and accordingly utilities, of VGR3051 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3051 gene: VGAM1420 host target protein, VGAM1421 host target protein, VGAM1422 host target protein and VGAM1423 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-

above with reference to VGAM1420, VGAM1421, VGAM1422 and VGAM1423. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3052 (VGR3052) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3301] VGR3052 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3052 gene was detected is described hereinabove with reference to Figs. 1-9.

[3302] VGR3052 gene encodes VGR3052 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3303] VGR3052 precursor RNA folds spatially, forming VGR3052 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3052 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3052 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3304] VGR3052 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1424 precursor RNA, VGAM1425 precursor RNA, VGAM1426 precursor RNA, VGAM1427 precursor RNA, VGAM1428 precursor RNA, VGAM1429 precursor RNA and VGAM1430 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3305] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1424 RNA, VGAM1425 RNA, VGAM1426 RNA, VGAM1427 RNA, VGAM1428 RNA, VGAM1429 RNA and VGAM1430 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to

VGAM RNA of Fig. 1.

[3306] VGAM1424 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1424 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1424 host target RNA into VGAM1424 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3307] VGAM1425 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1425 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1425 host target RNA into VGAM1425 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3308] VGAM1426 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1426 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1426 host target RNA into VGAM1426 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3309] VGAM1427 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1427 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1427 host target RNA into

VGAM1427 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3310] VGAM1428 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1428 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1428 host target RNA into VGAM1428 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3311] VGAM1429 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1429 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1429 host target RNA into VGAM1429 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3312] VGAM1430 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1430 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1430 host target RNA into VGAM1430 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3313] It is appreciated that a function of VGR3052 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3052 gene include diagnosis, prevention and treatment of viral infection by Clover Yellow Vein Virus. Specific functions, and accordingly utilities, of VGR3052 gene correlate with, and may

be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3052 gene: VGAM1424 host target protein, VGAM1425 host target protein, VGAM1426 host target protein, VGAM1427 host target protein, VGAM1428 host target protein, VGAM1429 host target protein and VGAM1430 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1424, VGAM1425, VGAM1426, VGAM1427, VGAM1428, VGAM1429 and VGAM1430. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3053(VGR3053) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3314] VGR3053 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3053 gene was

detected is described hereinabove with reference to Figs. 1-9.

[3315] VGR3053 gene encodes VGR3053 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3316] VGR3053 precursor RNA folds spatially, forming VGR3053 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3053 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3053 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3317] VGR3053 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1431 precursor RNA, VGAM1432 precursor RNA, VGAM1433 precursor RNA, VGAM1434 precursor RNA, VGAM1435 precursor RNA, VGAM1436 precursor RNA and VGAM1437 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3318] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1431 RNA, VGAM1432 RNA, VGAM1433 RNA, VGAM1434 RNA, VGAM1435 RNA, VGAM1436 RNA and VGAM1437 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3319] VGAM1431 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1431 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1431 host target RNA into VGAM1431 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3320] VGAM1432 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1432 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1432 host target RNA into VGAM1432 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3321] VGAM1433 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1433 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1433 host target RNA into VGAM1433 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3322] VGAM1434 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1434 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1434 host target RNA into VGAM1434 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3323] VGAM1435 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1435 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1435 host target RNA into

VGAM1435 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3324] VGAM1436 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1436 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1436 host target RNA into VGAM1436 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3325] VGAM1437 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1437 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1437 host target RNA into VGAM1437 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3326] It is appreciated that a function of VGR3053 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3053 gene include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGR3053 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3053 gene: VGAM1431 host target protein, VGAM1432 host target protein, VGAM1433 host target protein, VGAM1434 host target protein, VGAM1435 host target protein, VGAM1436 host target protein and VGAM1437 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1431, VGAM1432, VGAM1433, VGAM1434, VGAM1435, VGAM1436 and VGAM1437. Fig.

9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3054(VGR3054) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3327] VGR3054 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3054 gene was detected is described hereinabove with reference to Figs. 1-9.

[3328] VGR3054 gene encodes VGR3054 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3329] VGR3054 precursor RNA folds spatially, forming VGR3054 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3054 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3054 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3330] VGR3054 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1438 precursor RNA, VGAM1439 precursor RNA, VGAM1440 precursor RNA, VGAM1441 precursor RNA and VGAM1442 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3331] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1438 RNA, VGAM1439 RNA, VGAM1440 RNA, VGAM1441 RNA and VGAM1442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3332] VGAM1438 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1438 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1438 host target RNA into VGAM1438 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3333] VGAM1439 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1439 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1439 host target RNA into VGAM1439 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3334] VGAM1440 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1440 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1440 host target RNA into VGAM1440 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3335] VGAM1441 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1441 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1441 host target RNA into VGAM1441 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3336] VGAM1442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1442 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1442 host target RNA into VGAM1442 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3337] It is appreciated that a function of VGR3054 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3054 gene include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGR3054 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3054 gene: VGAM1438 host target protein, VGAM1439 host target protein,

VGAM1440 host target protein, VGAM1441 host target protein and VGAM1442 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1438, VGAM1439, VGAM1440, VGAM1441 and VGAM1442. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3055(VGR3055) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3338] VGR3055 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3055 gene was detected is described hereinabove with reference to Figs. 1-9.

[3339] VGR3055 gene encodes VGR3055 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3340] VGR3055 precursor RNA folds spatially, forming VGR3055

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3055 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3055 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3341] VGR3055 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1443 precursor RNA, VGAM1444 precursor RNA, VGAM1445 precursor RNA, VGAM1446 precursor RNA, VGAM1447 precursor RNA and VGAM1448 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3342] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1443

RNA, VGAM1444 RNA, VGAM1445 RNA, VGAM1446 RNA, VGAM1447 RNA and VGAM1448 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3343] VGAM1443 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1443 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1443 host target RNA into VGAM1443 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3344] VGAM1444 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1444 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1444 host target RNA into VGAM1444 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3345] VGAM1445 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1445 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1445 host target RNA into VGAM1445 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3346] VGAM1446 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1446 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1446 host target RNA into VGAM1446 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3347] VGAM1447 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1447 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1447 host target RNA into VGAM1447 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3348] VGAM1448 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1448 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1448 host target RNA into VGAM1448 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3349] It is appreciated that a function of VGR3055 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3055 gene include diagnosis, prevention and treatment of viral infection by Pepper Mottle Virus. Specific functions, and accordingly utilities, of VGR3055 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3055 gene: VGAM1443 host target protein, VGAM1444 host target protein, VGAM1445 host target protein, VGAM1446 host target protein, VGAM1447 host target protein and VGAM1448 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN.

The function of these host target genes is elaborated hereinabove with reference to VGAM1443, VGAM1444, VGAM1445, VGAM1446, VGAM1447 and VGAM1448. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3056(VGR3056) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3350] VGR3056 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3056 gene was detected is described hereinabove with reference to Figs. 1-9.

[3351] VGR3056 gene encodes VGR3056 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3352] VGR3056 precursor RNA folds spatially, forming VGR3056 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3056 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3056 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3353] VGR3056 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1449 precursor RNA, VGAM1450 precursor RNA, VGAM1451 precursor RNA, VGAM1452 precursor RNA, VGAM1453 precursor RNA, VGAM1454 precursor RNA, VGAM1455 precursor RNA and VGAM1456 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3354] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1449 RNA, VGAM1450 RNA, VGAM1451 RNA, VGAM1452 RNA, VGAM1453 RNA, VGAM1454 RNA, VGAM1455 RNA and

VGAM1456 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3355] VGAM1449 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1449 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1449 host target RNA into VGAM1449 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3356] VGAM1450 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1450 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1450 host target RNA into VGAM1450 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3357] VGAM1451 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1451 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1451 host target RNA into VGAM1451 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3358] VGAM1452 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1452 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1452 host target RNA into VGAM1452 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3359] VGAM1453 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1453 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1453 host target RNA into VGAM1453 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3360] VGAM1454 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1454 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1454 host target RNA into VGAM1454 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3361] VGAM1455 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1455 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1455 host target RNA into VGAM1455 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3362] VGAM1456 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1456 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1456 host target RNA into VGAM1456 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3363] It is appreciated that a function of VGR3056 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3056 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3056 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3056 gene: VGAM1449 host target protein, VGAM1450 host target protein, VGAM1451 host target protein, VGAM1452 host target protein, VGAM1453 host target protein, VGAM1454 host target protein, VGAM1455 host target protein and VGAM1456 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1449, VGAM1450, VGAM1451, VGAM1452, VGAM1453, VGAM1454, VGAM1455 and VGAM1456. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3057 (VGR3057) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3364] VGR3057 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3057 gene was detected is described hereinabove with reference to Figs. 1-9.

[3365] VGR3057 gene encodes VGR3057 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3366] VGR3057 precursor RNA folds spatially, forming VGR3057 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3057 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3057 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3367] VGR3057 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1457 precursor RNA, VGAM1458 precursor RNA, VGAM1459 precursor RNA, VGAM1460 precursor RNA, VGAM1461 precursor RNA, VGAM1462 precursor RNA, VGAM1463 precursor RNA and VGAM1464 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3368] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1457 RNA, VGAM1458 RNA, VGAM1459 RNA, VGAM1460 RNA, VGAM1461 RNA, VGAM1462 RNA, VGAM1463 RNA and

VGAM1464 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3369] VGAM1457 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1457 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1457 host target RNA into VGAM1457 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3370] VGAM1458 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1458 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1458 host target RNA into VGAM1458 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3371] VGAM1459 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1459 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1459 host target RNA into VGAM1459 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3372] VGAM1460 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1460 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1460 host target RNA into VGAM1460 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3373] VGAM1461 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1461 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1461 host target RNA into VGAM1461 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3374] VGAM1462 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1462 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1462 host target RNA into VGAM1462 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3375] VGAM1463 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1463 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1463 host target RNA into VGAM1463 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3376] VGAM1464 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1464 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1464 host target RNA into VGAM1464 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3377] It is appreciated that a function of VGR3057 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3057 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3057 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3057 gene: VGAM1457 host target protein, VGAM1458 host target protein, VGAM1459 host target protein, VGAM1460 host target protein, VGAM1461 host target protein, VGAM1462 host target protein, VGAM1463 host target protein and VGAM1464 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1457, VGAM1458, VGAM1459, VGAM1460, VGAM1461, VGAM1462, VGAM1463 and VGAM1464. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3058 (VGR3058) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3378] VGR3058 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3058 gene was detected is described hereinabove with reference to Figs. 1-9.

[3379] VGR3058 gene encodes VGR3058 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3380] VGR3058 precursor RNA folds spatially, forming VGR3058 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3058 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3058 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3381] VGR3058 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1465 precursor RNA, VGAM1466 precursor RNA and VGAM1467 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3382] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1465 RNA, VGAM1466 RNA and VGAM1467 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3383] VGAM1465 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1465 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1465 host target RNA into VGAM1465 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3384] VGAM1466 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1466 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1466 host target RNA into VGAM1466 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3385] VGAM1467 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1467 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1467 host target RNA into VGAM1467 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3386] It is appreciated that a function of VGR3058 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3058 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3058 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3058 gene: VGAM1465 host

target protein, VGAM1466 host target protein and VGAM1467 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1465, VGAM1466 and VGAM1467. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3059(VGR3059) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3387] VGR3059 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3059 gene was detected is described hereinabove with reference to Figs. 1-9.

[3388] VGR3059 gene encodes VGR3059 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3389] VGR3059 precursor RNA folds spatially, forming VGR3059

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3059 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3059 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3390] VGR3059 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1468 precursor RNA and VGAM1469 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3391] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1468 RNA and VGAM1469 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of

which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3392] VGAM1468 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1468 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1468 host target RNA into VGAM1468 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3393] VGAM1469 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1469 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1469 host target RNA into VGAM1469 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3394] It is appreciated that a function of VGR3059 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3059 gene include diagnosis, prevention and treatment of viral infection by Infectious Flacherie Virus. Specific functions, and accordingly utilities, of VGR3059 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3059 gene: VGAM1468 host target protein and VGAM1469 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1468 and VGAM1469. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3060(VGR3060) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[3395] VGR3060 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3060 gene was detected is described hereinabove with reference to Figs. 1-9.

[3396] VGR3060 gene encodes VGR3060 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3397] VGR3060 precursor RNA folds spatially, forming VGR3060 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3060 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3060 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3398] VGR3060 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM

precursor RNAs, VGAM1470 precursor RNA, VGAM1471 precursor RNA, VGAM1472 precursor RNA, VGAM1473 precursor RNA, VGAM1474 precursor RNA, VGAM1475 precursor RNA, VGAM1476 precursor RNA and VGAM1477 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3399] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1470 RNA, VGAM1471 RNA, VGAM1472 RNA, VGAM1473 RNA, VGAM1474 RNA, VGAM1475 RNA, VGAM1476 RNA and VGAM1477 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3400] VGAM1470 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1470 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1470 host target RNA into VGAM1470 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3401] VGAM1471 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1471 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1471 host target RNA into VGAM1471 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3402] VGAM1472 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1472 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1472 host target RNA into VGAM1472 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3403] VGAM1473 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1473 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1473 host target RNA into VGAM1473 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3404] VGAM1474 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1474 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1474 host target RNA into VGAM1474 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3405] VGAM1475 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1475 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1475 host target RNA into VGAM1475 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3406] VGAM1476 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1476 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1476 host target RNA into VGAM1476 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3407] VGAM1477 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1477 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1477 host target RNA into VGAM1477 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3408] It is appreciated that a function of VGR3060 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3060 gene include diagnosis, prevention and treatment of viral infection by Cocksfoot Streak Virus (CSV). Specific functions, and accordingly utilities, of VGR3060 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3060 gene: VGAM1470 host target protein, VGAM1471 host target protein, VGAM1472 host target protein, VGAM1473 host target protein, VGAM1474 host target protein, VGAM1475 host target protein, VGAM1476 host target protein and VGAM1477 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1470, VGAM1471, VGAM1472, VGAM1473, VGAM1474, VGAM1475, VGAM1476 and VGAM1477. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3061(VGR3061) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates

expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3409] VGR3061 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3061 gene was detected is described hereinabove with reference to Figs. 1-9.

[3410] VGR3061 gene encodes VGR3061 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3411] VGR3061 precursor RNA folds spatially, forming VGR3061 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3061 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3061 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3412] VGR3061 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1478 precursor RNA, VGAM1479 precursor RNA, VGAM1480 precursor RNA, VGAM1481 precursor RNA, VGAM1482 precursor RNA and VGAM1483 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3413] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1478 RNA, VGAM1479 RNA, VGAM1480 RNA, VGAM1481 RNA, VGAM1482 RNA and VGAM1483 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3414] VGAM1478 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1478 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1478 host target RNA into VGAM1478 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3415] VGAM1479 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1479 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1479 host target RNA into VGAM1479 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3416] VGAM1480 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1480 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1480 host target RNA into VGAM1480 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3417] VGAM1481 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1481 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1481 host target RNA into VGAM1481 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3418] VGAM1482 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1482 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1482 host target RNA into VGAM1482 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3419] VGAM1483 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1483 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1483 host target RNA into VGAM1483 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3420] It is appreciated that a function of VGR3061 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3061 gene include diagnosis, prevention and treatment of viral infection by Brome Streak Mosaic Virus. Specific functions, and accordingly utilities, of VGR3061 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3061 gene: VGAM1478 host target protein, VGAM1479 host target protein, VGAM1480 host target protein, VGAM1481 host target protein, VGAM1482 host target protein and VGAM1483 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1478, VGAM1479, VGAM1480, VGAM1481, VGAM1482 and VGAM1483. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3062(VGR3062) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3421] VGR3062 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3062 gene was detected is described hereinabove with reference to Figs. 1–9.

[3422] VGR3062 gene encodes VGR3062 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3423] VGR3062 precursor RNA folds spatially, forming VGR3062 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3062 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3062 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[3424] VGR3062 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1484 precursor RNA, VGAM1485 precursor RNA, VGAM1486 precursor RNA and VGAM1487

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3425] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1484 RNA, VGAM1485 RNA, VGAM1486 RNA and VGAM1487 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3426] VGAM1484 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1484 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1484 host target RNA into VGAM1484 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3427] VGAM1485 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1485 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1485 host target RNA into VGAM1485 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3428] VGAM1486 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1486 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1486 host target RNA into VGAM1486 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3429] VGAM1487 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1487 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1487 host target RNA into VGAM1487 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3430] It is appreciated that a function of VGR3062 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3062 gene include diagnosis, prevention and treatment of viral infection by Gallid Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3062 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3062 gene: VGAM1484 host target protein, VGAM1485 host target protein, VGAM1486 host target protein and VGAM1487 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1484, VGAM1485, VGAM1486 and VGAM1487. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3063(VGR3063) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3431] VGR3063 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3063 gene was detected is described hereinabove with reference to Figs. 1-9.

[3432] VGR3063 gene encodes VGR3063 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3433] VGR3063 precursor RNA folds spatially, forming VGR3063 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3063 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3063 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3434] VGR3063 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1488 precursor RNA, VGAM1489 precursor RNA, VGAM1490 precursor RNA and VGAM1491 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3435] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1488

RNA, VGAM1489 RNA, VGAM1490 RNA and VGAM1491 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3436] VGAM1488 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1488 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1488 host target RNA into VGAM1488 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3437] VGAM1489 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1489 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1489 host target RNA into VGAM1489 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3438] VGAM1490 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1490 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1490 host target RNA into VGAM1490 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3439] VGAM1491 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1491 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1491 host target RNA into VGAM1491 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3440] It is appreciated that a function of VGR3063 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3063 gene include diagnosis, prevention and treatment of viral infection by Plum Pox Virus. Specific functions, and accordingly utilities, of VGR3063 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3063 gene: VGAM1488 host target protein, VGAM1489 host target protein, VGAM1490 host target protein and VGAM1491 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1488, VGAM1489, VGAM1490 and VGAM1491. Fig. 9 further provides a con-

ceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3064(VGR3064) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3441] VGR3064 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3064 gene was detected is described hereinabove with reference to Figs. 1-9.

[3442] VGR3064 gene encodes VGR3064 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3443] VGR3064 precursor RNA folds spatially, forming VGR3064 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3064 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3064 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3444] VGR3064 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1492 precursor RNA, VGAM1493 precursor RNA, VGAM1494 precursor RNA and VGAM1495 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3445] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1492 RNA, VGAM1493 RNA, VGAM1494 RNA and VGAM1495 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3446] VGAM1492 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1492 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1492 host target RNA into VGAM1492 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3447] VGAM1493 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1493 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1493 host target RNA into VGAM1493 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3448] VGAM1494 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1494 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1494 host target RNA into VGAM1494 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3449] VGAM1495 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1495 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1495 host target RNA into VGAM1495 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3450] It is appreciated that a function of VGR3064 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3064 gene include diagnosis, prevention and treatment of viral infection by Johnsongrass Mosaic Virus. Specific functions, and accordingly utilities, of VGR3064 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3064 gene: VGAM1492 host target protein, VGAM1493 host target protein, VGAM1494 host target protein and VGAM1495 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1492, VGAM1493, VGAM1494 and VGAM1495. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3065(VGR3065) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3451] VGR3065 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3065 gene was detected is described hereinabove with reference to Figs. 1-9.

[3452] VGR3065 gene encodes VGR3065 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3453] VGR3065 precursor RNA folds spatially, forming VGR3065 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3065 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3065 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3454] VGR3065 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1496 precursor RNA, VGAM1497 precursor RNA, VGAM1498 precursor RNA and VGAM1499 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3455] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1496 RNA, VGAM1497 RNA, VGAM1498 RNA and VGAM1499 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3456] VGAM1496 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1496 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1496 host target RNA into VGAM1496 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3457] VGAM1497 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1497 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1497 host target RNA into VGAM1497 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3458] VGAM1498 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1498 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1498 host target RNA into VGAM1498 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3459] VGAM1499 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1499 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1499 host target RNA into VGAM1499 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3460] It is appreciated that a function of VGR3065 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3065 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3065 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3065 gene: VGAM1496 host

target protein, VGAM1497 host target protein, VGAM1498 host target protein and VGAM1499 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM1496, VGAM1497, VGAM1498 and VGAM1499. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3066(VGR3066) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3461] VGR3066 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3066 gene was detected is described hereinabove with reference to Figs. 1–9.

[3462] VGR3066 gene encodes VGR3066 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3463] VGR3066 precursor RNA folds spatially, forming VGR3066

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3066 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3066 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3464] VGR3066 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1500 precursor RNA, VGAM1501 precursor RNA, VGAM1502 precursor RNA, VGAM1503 precursor RNA, VGAM1504 precursor RNA, VGAM1505 precursor RNA, VGAM1506 precursor RNA and VGAM1507 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3465] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1500 RNA, VGAM1501 RNA, VGAM1502 RNA, VGAM1503 RNA, VGAM1504 RNA, VGAM1505 RNA, VGAM1506 RNA and VGAM1507 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3466] VGAM1500 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1500 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1500 host target RNA into VGAM1500 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3467] VGAM1501 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1501 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1501 host target RNA into VGAM1501 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3468] VGAM1502 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1502 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1502 host target RNA into VGAM1502 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3469] VGAM1503 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1503 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1503 host target RNA into VGAM1503 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3470] VGAM1504 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1504 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1504 host target RNA into VGAM1504 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3471] VGAM1505 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1505 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1505 host target RNA into VGAM1505 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3472] VGAM1506 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1506 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1506 host target RNA into VGAM1506 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3473] VGAM1507 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1507 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1507 host target RNA into VGAM1507 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3474] It is appreciated that a function of VGR3066 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3066 gene include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGR3066 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3066 gene: VGAM1500 host target protein, VGAM1501 host target protein, VGAM1502 host target protein, VGAM1503 host target protein, VGAM1504 host target protein, VGAM1505 host

target protein, VGAM1506 host target protein and VGAM1507 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1500, VGAM1501, VGAM1502, VGAM1503, VGAM1504, VGAM1505, VGAM1506 and VGAM1507. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3067(VGR3067) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3475] VGR3067 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3067 gene was detected is described hereinabove with reference to Figs. 1-9.

[3476] VGR3067 gene encodes VGR3067 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3477] VGR3067 precursor RNA folds spatially, forming VGR3067 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3067 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3067 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3478] VGR3067 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1508 precursor RNA, VGAM1509 precursor RNA, VGAM1510 precursor RNA and VGAM1511 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3479] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1508

RNA, VGAM1509 RNA, VGAM1510 RNA and VGAM1511 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3480] VGAM1508 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1508 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1508 host target RNA into VGAM1508 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3481] VGAM1509 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1509 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1509 host target RNA into VGAM1509 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3482] VGAM1510 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1510 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1510 host target RNA into VGAM1510 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3483] VGAM1511 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1511 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1511 host target RNA into VGAM1511 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3484] It is appreciated that a function of VGR3067 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3067 gene include diagnosis, prevention and treatment of viral infection by Potato Virus V. Specific functions, and accordingly utilities, of VGR3067 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3067 gene: VGAM1508 host target protein, VGAM1509 host target protein, VGAM1510 host target protein and VGAM1511 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1508, VGAM1509, VGAM1510 and VGAM1511. Fig. 9 further provides a con-

ceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3068(VGR3068) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3485] VGR3068 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3068 gene was detected is described hereinabove with reference to Figs. 1-9.

[3486] VGR3068 gene encodes VGR3068 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3487] VGR3068 precursor RNA folds spatially, forming VGR3068 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3068 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3068 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3488] VGR3068 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1512 precursor RNA, VGAM1513 precursor RNA, VGAM1514 precursor RNA, VGAM1515 precursor RNA and VGAM1516 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3489] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1512 RNA, VGAM1513 RNA, VGAM1514 RNA, VGAM1515 RNA and VGAM1516 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3490] VGAM1512 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1512 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1512 host target RNA into VGAM1512 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3491] VGAM1513 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1513 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1513 host target RNA into VGAM1513 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3492] VGAM1514 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1514 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1514 host target RNA into VGAM1514 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3493] VGAM1515 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1515 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1515 host target RNA into VGAM1515 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3494] VGAM1516 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1516 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1516 host target RNA into VGAM1516 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3495] It is appreciated that a function of VGR3068 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3068 gene include diagnosis, prevention and treatment of viral infection by Parsnip Yellow Fleck Virus. Specific functions, and accordingly utilities, of VGR3068 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3068 gene: VGAM1512 host target protein, VGAM1513 host target protein, VGAM1514 host target protein, VGAM1515 host target protein and

VGAM1516 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1512, VGAM1513, VGAM1514, VGAM1515 and VGAM1516. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3069(VGR3069) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3496] VGR3069 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3069 gene was detected is described hereinabove with reference to Figs. 1-9.

[3497] VGR3069 gene encodes VGR3069 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3498] VGR3069 precursor RNA folds spatially, forming VGR3069 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3069 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3069 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3499] VGR3069 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1517 precursor RNA, VGAM1518 precursor RNA and VGAM1519 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3500] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1517 RNA, VGAM1518 RNA and VGAM1519 RNA, herein schematically represented by VGAM1 RNA through VGAM3

RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3501] VGAM1517 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1517 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1517 host target RNA into VGAM1517 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3502] VGAM1518 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1518 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1518 host target RNA into

VGAM1518 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3503] VGAM1519 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1519 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1519 host target RNA into VGAM1519 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3504] It is appreciated that a function of VGR3069 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3069 gene include diagnosis, prevention and treatment of viral infection by Pea Seed-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGR3069 gene correlate with, and may be deduced from, the identity of the host target

genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3069 gene: VGAM1517 host target protein, VGAM1518 host target protein and VGAM1519 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1517, VGAM1518 and VGAM1519. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3070(VGR3070) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3505] VGR3070 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3070 gene was detected is described hereinabove with reference to Figs. 1-9.

[3506] VGR3070 gene encodes VGR3070 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[3507] VGR3070 precursor RNA folds spatially, forming VGR3070 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3070 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3070 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3508] VGR3070 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1520 precursor RNA, VGAM1521 precursor RNA, VGAM1522 precursor RNA, VGAM1523 precursor RNA, VGAM1524 precursor RNA, VGAM1525 precursor RNA, VGAM1526 precursor RNA and VGAM1527 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3509] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1520 RNA, VGAM1521 RNA, VGAM1522 RNA, VGAM1523 RNA, VGAM1524 RNA, VGAM1525 RNA, VGAM1526 RNA and VGAM1527 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3510] VGAM1520 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1520 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1520 host target RNA into VGAM1520 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3511] VGAM1521 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1521 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1521 host target RNA into VGAM1521 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3512] VGAM1522 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1522 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1522 host target RNA into VGAM1522 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3513] VGAM1523 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1523 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1523 host target RNA into VGAM1523 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3514] VGAM1524 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1524 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1524 host target RNA into VGAM1524 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3515] VGAM1525 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1525 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1525 host target RNA into VGAM1525 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3516] VGAM1526 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1526 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1526 host target RNA into VGAM1526 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3517] VGAM1527 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1527 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1527 host target RNA into VGAM1527 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3518] It is appreciated that a function of VGR3070 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3070 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3070 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3070 gene: VGAM1520 host target protein, VGAM1521 host target protein, VGAM1522

host target protein, VGAM1523 host target protein, VGAM1524 host target protein, VGAM1525 host target protein, VGAM1526 host target protein and VGAM1527 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1520, VGAM1521, VGAM1522, VGAM1523, VGAM1524, VGAM1525, VGAM1526 and VGAM1527. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3071 (VGR3071) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3519] VGR3071 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3071 gene was detected is described hereinabove with reference to Figs. 1-9.

[3520] VGR3071 gene encodes VGR3071 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[3521] VGR3071 precursor RNA folds spatially, forming VGR3071 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3071 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3071 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3522] VGR3071 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1528 precursor RNA, VGAM1529 precursor RNA, VGAM1530 precursor RNA and VGAM1531 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3523] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1528 RNA, VGAM1529 RNA, VGAM1530 RNA and VGAM1531 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3524] VGAM1528 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1528 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1528 host target RNA into VGAM1528 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3525] VGAM1529 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1529 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1529 host target RNA into VGAM1529 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3526] VGAM1530 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1530 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1530 host target RNA into VGAM1530 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3527] VGAM1531 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1531 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1531 host target RNA into VGAM1531 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3528] It is appreciated that a function of VGR3071 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3071 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3071 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3071 gene: VGAM1528 host target protein, VGAM1529 host target protein, VGAM1530 host target protein and VGAM1531 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1528, VGAM1529,

VGAM1530 and VGAM1531. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3072 (VGR3072) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3529] VGR3072 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3072 gene was detected is described hereinabove with reference to Figs. 1-9.

[3530] VGR3072 gene encodes VGR3072 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3531] VGR3072 precursor RNA folds spatially, forming VGR3072 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3072 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3072 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3532] VGR3072 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1532 precursor RNA, VGAM1533 precursor RNA, VGAM1534 precursor RNA, VGAM1535 precursor RNA, VGAM1536 precursor RNA and VGAM1537 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3533] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1532 RNA, VGAM1533 RNA, VGAM1534 RNA, VGAM1535 RNA, VGAM1536 RNA and VGAM1537 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3534] VGAM1532 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1532 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1532 host target RNA into VGAM1532 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3535] VGAM1533 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1533 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1533 host target RNA into VGAM1533 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3536] VGAM1534 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1534 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1534 host target RNA into VGAM1534 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3537] VGAM1535 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1535 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1535 host target RNA into VGAM1535 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3538] VGAM1536 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1536 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1536 host target RNA into VGAM1536 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3539] VGAM1537 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1537 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1537 host target RNA into VGAM1537 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3540] It is appreciated that a function of VGR3072 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3072 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR3072 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3072 gene: VGAM1532 host target protein, VGAM1533 host target protein, VGAM1534 host target protein, VGAM1535 host target protein, VGAM1536 host target protein and VGAM1537 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1532, VGAM1533, VGAM1534, VGAM1535, VGAM1536 and VGAM1537. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3073(VGR3073) viral gene, which en-

codes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3541] VGR3073 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3073 gene was detected is described hereinabove with reference to Figs. 1-9.

[3542] VGR3073 gene encodes VGR3073 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3543] VGR3073 precursor RNA folds spatially, forming VGR3073 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3073 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3073 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3544] VGR3073 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1538 precursor RNA, VGAM1539 precursor RNA, VGAM1540 precursor RNA and VGAM1541 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3545] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1538 RNA, VGAM1539 RNA, VGAM1540 RNA and VGAM1541 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3546] VGAM1538 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1538 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1538 host target RNA into VGAM1538 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3547] VGAM1539 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1539 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1539 host target RNA into VGAM1539 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3548] VGAM1540 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1540 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1540 host target RNA into VGAM1540 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3549] VGAM1541 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1541 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1541 host target RNA into VGAM1541 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3550] It is appreciated that a function of VGR3073 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3073 gene include diagnosis, prevention and treatment of viral infection by

Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3073 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3073 gene: VGAM1538 host target protein, VGAM1539 host target protein, VGAM1540 host target protein and VGAM1541 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1538, VGAM1539, VGAM1540 and VGAM1541. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3074(VGR3074) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3551] VGR3074 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3074 gene was detected is described hereinabove with reference to Figs.

1-9.

[3552] VGR3074 gene encodes VGR3074 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3553] VGR3074 precursor RNA folds spatially, forming VGR3074 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3074 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3074 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3554] VGR3074 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1542 precursor RNA, VGAM1543 precursor RNA, VGAM1544 precursor RNA, VGAM1545 precursor RNA, VGAM1546 precursor RNA and VGAM1547 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3555] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1542 RNA, VGAM1543 RNA, VGAM1544 RNA, VGAM1545 RNA, VGAM1546 RNA and VGAM1547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3556] VGAM1542 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1542 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1542 host target RNA into VGAM1542 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3557] VGAM1543 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1543 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1543 host target RNA into VGAM1543 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3558] VGAM1544 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1544 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1544 host target RNA into VGAM1544 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3559] VGAM1545 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1545 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1545 host target RNA into VGAM1545 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3560] VGAM1546 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1546 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1546 host target RNA into VGAM1546 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3561] VGAM1547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1547 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1547 host target RNA into VGAM1547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3562] It is appreciated that a function of VGR3074 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3074 gene include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR3074 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3074 gene: VGAM1542 host target protein,

VGAM1543 host target protein, VGAM1544 host target protein, VGAM1545 host target protein, VGAM1546 host target protein and VGAM1547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1542, VGAM1543, VGAM1544, VGAM1545, VGAM1546 and VGAM1547. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3075 (VGR3075) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3563] VGR3075 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3075 gene was detected is described hereinabove with reference to Figs. 1-9.

[3564] VGR3075 gene encodes VGR3075 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3565] VGR3075 precursor RNA folds spatially, forming VGR3075 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3075 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3075 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3566] VGR3075 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1548 precursor RNA, VGAM1549 precursor RNA, VGAM1550 precursor RNA, VGAM1551 precursor RNA, VGAM1552 precursor RNA, VGAM1553 precursor RNA, VGAM1554 precursor RNA and VGAM1555 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3567] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1548 RNA, VGAM1549 RNA, VGAM1550 RNA, VGAM1551 RNA, VGAM1552 RNA, VGAM1553 RNA, VGAM1554 RNA and VGAM1555 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3568] VGAM1548 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1548 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1548 host target RNA into VGAM1548 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3569] VGAM1549 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1549 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1549 host target RNA into VGAM1549 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3570] VGAM1550 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1550 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1550 host target RNA into VGAM1550 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3571] VGAM1551 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1551 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1551 host target RNA into VGAM1551 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3572] VGAM1552 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1552 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1552 host target RNA into VGAM1552 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3573] VGAM1553 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1553 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1553 host target RNA into VGAM1553 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3574] VGAM1554 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1554 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1554 host target RNA into VGAM1554 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3575] VGAM1555 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1555 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1555 host target RNA into VGAM1555 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3576] It is appreciated that a function of VGR3075 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3075 gene include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGR3075 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3075 gene: VGAM1548 host target protein, VGAM1549 host target protein, VGAM1550 host target protein, VGAM1551 host target

protein, VGAM1552 host target protein, VGAM1553 host target protein, VGAM1554 host target protein and VGAM1555 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1548, VGAM1549, VGAM1550, VGAM1551, VGAM1552, VGAM1553, VGAM1554 and VGAM1555. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3076(VGR3076) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3577] VGR3076 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3076 gene was detected is described hereinabove with reference to Figs. 1-9.

[3578] VGR3076 gene encodes VGR3076 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[3579] VGR3076 precursor RNA folds spatially, forming VGR3076 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3076 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3076 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3580] VGR3076 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1556 precursor RNA and VGAM1557 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3581] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1556

RNA and VGAM1557 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3582] VGAM1556 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1556 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1556 host target RNA into VGAM1556 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3583] VGAM1557 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1557 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1557 host target RNA into VGAM1557 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3584] It is appreciated that a function of VGR3076 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3076 gene include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGR3076 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3076 gene: VGAM1556 host target protein and VGAM1557 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1556 and VGAM1557. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3077(VGR3077) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3585] VGR3077 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3077 gene was detected is described hereinabove with reference to Figs. 1-9.

[3586] VGR3077 gene encodes VGR3077 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3587] VGR3077 precursor RNA folds spatially, forming VGR3077 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3077 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3077 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3588] VGR3077 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1558 precursor RNA, VGAM1559 precursor RNA, VGAM1560 precursor RNA, VGAM1561 precursor RNA, VGAM1562 precursor RNA and VGAM1563 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3589] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1558 RNA, VGAM1559 RNA, VGAM1560 RNA, VGAM1561 RNA, VGAM1562 RNA and VGAM1563 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3590] VGAM1558 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1558 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1558 host target RNA into VGAM1558 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3591] VGAM1559 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1559 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1559 host target RNA into VGAM1559 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3592] VGAM1560 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1560 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1560 host target RNA into VGAM1560 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3593] VGAM1561 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1561 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1561 host target RNA into VGAM1561 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3594] VGAM1562 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1562 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1562 host target RNA into VGAM1562 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3595] VGAM1563 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1563 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1563 host target RNA into VGAM1563 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3596] It is appreciated that a function of VGR3077 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3077 gene include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Virus. Specific functions, and accordingly utilities, of VGR3077 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3077 gene: VGAM1558 host target protein, VGAM1559 host target protein, VGAM1560 host target protein, VGAM1561 host target protein, VGAM1562 host target protein and VGAM1563 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1558, VGAM1559, VGAM1560, VGAM1561, VGAM1562 and VGAM1563. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3078(VGR3078) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least

one host target gene is known in the art.

[3597] VGR3078 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3078 gene was detected is described hereinabove with reference to Figs. 1-9.

[3598] VGR3078 gene encodes VGR3078 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3599] VGR3078 precursor RNA folds spatially, forming VGR3078 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3078 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3078 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3600] VGR3078 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1564 precursor RNA, VGAM1565

precursor RNA and VGAM1566 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3601] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1564 RNA, VGAM1565 RNA and VGAM1566 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3602] VGAM1564 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1564 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1564 host target RNA into VGAM1564 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3603] VGAM1565 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1565 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1565 host target RNA into VGAM1565 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3604] VGAM1566 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1566 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1566 host target RNA into

VGAM1566 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3605] It is appreciated that a function of VGR3078 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3078 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGR3078 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3078 gene: VGAM1564 host target protein, VGAM1565 host target protein and VGAM1566 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1564, VGAM1565 and VGAM1566. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3079(VGR3079) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3606] VGR3079 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3079 gene was detected is described hereinabove with reference to Figs. 1-9.

[3607] VGR3079 gene encodes VGR3079 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3608] VGR3079 precursor RNA folds spatially, forming VGR3079 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3079 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3079 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3609] VGR3079 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1567 precursor RNA, VGAM1568 precursor RNA, VGAM1569 precursor RNA and VGAM1570 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3610] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1567 RNA, VGAM1568 RNA, VGAM1569 RNA and VGAM1570 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3611] VGAM1567 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1567 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1567 host target RNA into VGAM1567 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3612] VGAM1568 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1568 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1568 host target RNA into VGAM1568 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3613] VGAM1569 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1569 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1569 host target RNA into VGAM1569 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3614] VGAM1570 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1570 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1570 host target RNA into VGAM1570 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3615] It is appreciated that a function of VGR3079 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3079 gene include diagnosis, prevention and treatment of viral infection by

Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGR3079 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3079 gene: VGAM1567 host target protein, VGAM1568 host target protein, VGAM1569 host target protein and VGAM1570 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1567, VGAM1568, VGAM1569 and VGAM1570. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3080(VGR3080) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3616] VGR3080 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3080 gene was detected is described hereinabove with reference to Figs.

1-9.

- [3617] VGR3080 gene encodes VGR3080 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [3618] VGR3080 precursor RNA folds spatially, forming VGR3080 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3080 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3080 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [3619] VGR3080 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1571 precursor RNA, VGAM1572 precursor RNA, VGAM1573 precursor RNA, VGAM1574 precursor RNA, VGAM1575 precursor RNA, VGAM1576 precursor RNA, VGAM1577 precursor RNA and VGAM1578 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3620] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1571 RNA, VGAM1572 RNA, VGAM1573 RNA, VGAM1574 RNA, VGAM1575 RNA, VGAM1576 RNA, VGAM1577 RNA and VGAM1578 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3621] VGAM1571 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1571 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1571 host target RNA into VGAM1571 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3622] VGAM1572 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1572 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1572 host target RNA into VGAM1572 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3623] VGAM1573 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1573 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1573 host target RNA into VGAM1573 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3624] VGAM1574 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1574 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1574 host target RNA into VGAM1574 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3625] VGAM1575 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1575 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1575 host target RNA into VGAM1575 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3626] VGAM1576 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1576 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1576 host target RNA into VGAM1576 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3627] VGAM1577 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1577 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1577 host target RNA into

VGAM1577 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3628] VGAM1578 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1578 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1578 host target RNA into VGAM1578 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3629] It is appreciated that a function of VGR3080 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3080 gene include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGR3080 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3080 gene: VGAM1571 host
target protein, VGAM1572 host target protein, VGAM1573
host target protein, VGAM1574 host target protein,
VGAM1575 host target protein, VGAM1576 host target
protein, VGAM1577 host target protein and VGAM1578
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM1571,
VGAM1572, VGAM1573, VGAM1574, VGAM1575,
VGAM1576, VGAM1577 and VGAM1578. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3081(VGR3081) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[3630] VGR3081 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3081 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [3631] VGR3081 gene encodes VGR3081 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [3632] VGR3081 precursor RNA folds spatially, forming VGR3081 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3081 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3081 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [3633] VGR3081 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1579 precursor RNA and VGAM1580 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [3634] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1579 RNA and VGAM1580 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [3635] VGAM1579 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1579 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1579 host target RNA into VGAM1579 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [3636] VGAM1580 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1580 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1580 host target RNA into VGAM1580 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3637] It is appreciated that a function of VGR3081 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3081 gene include diagnosis, prevention and treatment of viral infection by Rhopalosiphum Padi Virus. Specific functions, and accordingly utilities, of VGR3081 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3081 gene: VGAM1579 host target protein and VGAM1580 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1579 and VGAM1580. Fig. 9 further provides a conceptual description of novel bioinfor-

matically detected regulatory viral gene, referred to here as Viral Genomic Record 3082(VGR3082) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3638] VGR3082 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3082 gene was detected is described hereinabove with reference to Figs. 1-9.

[3639] VGR3082 gene encodes VGR3082 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3640] VGR3082 precursor RNA folds spatially, forming VGR3082 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3082 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3082 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3641] VGR3082 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1581 precursor RNA, VGAM1582 precursor RNA, VGAM1583 precursor RNA, VGAM1584 precursor RNA, VGAM1585 precursor RNA, VGAM1586 precursor RNA, VGAM1587 precursor RNA and VGAM1588 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3642] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1581 RNA, VGAM1582 RNA, VGAM1583 RNA, VGAM1584 RNA, VGAM1585 RNA, VGAM1586 RNA, VGAM1587 RNA and VGAM1588 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3643] VGAM1581 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1581 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1581 host target RNA into VGAM1581 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3644] VGAM1582 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1582 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1582 host target RNA into VGAM1582 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3645] VGAM1583 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1583 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1583 host target RNA into VGAM1583 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3646] VGAM1584 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1584 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1584 host target RNA into VGAM1584 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3647] VGAM1585 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1585 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1585 host target RNA into VGAM1585 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3648] VGAM1586 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1586 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1586 host target RNA into VGAM1586 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3649] VGAM1587 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1587 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1587 host target RNA into VGAM1587 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3650] VGAM1588 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1588 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1588 host target RNA into

VGAM1588 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3651] It is appreciated that a function of VGR3082 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3082 gene include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3082 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3082 gene: VGAM1581 host target protein, VGAM1582 host target protein, VGAM1583 host target protein, VGAM1584 host target protein, VGAM1585 host target protein, VGAM1586 host target protein, VGAM1587 host target protein and VGAM1588 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1581, VGAM1582, VGAM1583, VGAM1584, VGAM1585, VGAM1586, VGAM1587 and VGAM1588. Fig. 9 further

provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3083(VGR3083) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3652] VGR3083 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3083 gene was detected is described hereinabove with reference to Figs. 1-9.

[3653] VGR3083 gene encodes VGR3083 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3654] VGR3083 precursor RNA folds spatially, forming VGR3083 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3083 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3083 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3655] VGR3083 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1589 precursor RNA, VGAM1590 precursor RNA, VGAM1591 precursor RNA, VGAM1592 precursor RNA and VGAM1593 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3656] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1589 RNA, VGAM1590 RNA, VGAM1591 RNA, VGAM1592 RNA and VGAM1593 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3657] VGAM1589 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1589 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1589 host target RNA into VGAM1589 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3658] VGAM1590 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1590 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1590 host target RNA into VGAM1590 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3659] VGAM1591 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1591 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1591 host target RNA into VGAM1591 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3660] VGAM1592 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1592 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1592 host target RNA into VGAM1592 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3661] VGAM1593 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1593 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1593 host target RNA into VGAM1593 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3662] It is appreciated that a function of VGR3083 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3083 gene include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3083 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3083 gene: VGAM1589 host target protein, VGAM1590 host target protein, VGAM1591 host target protein, VGAM1592 host target protein and

VGAM1593 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1589, VGAM1590, VGAM1591, VGAM1592 and VGAM1593. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3084(VGR3084) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3663] VGR3084 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3084 gene was detected is described hereinabove with reference to Figs. 1-9.

[3664] VGR3084 gene encodes VGR3084 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3665] VGR3084 precursor RNA folds spatially, forming VGR3084 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3084 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3084 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3666] VGR3084 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1594 precursor RNA, VGAM1595 precursor RNA, VGAM1596 precursor RNA and VGAM1597 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3667] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1594 RNA, VGAM1595 RNA, VGAM1596 RNA and VGAM1597 RNA, herein schematically represented by VGAM1 RNA

through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3668] VGAM1594 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1594 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1594 host target RNA into VGAM1594 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3669] VGAM1595 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1595 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1595 host target RNA into

VGAM1595 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3670] VGAM1596 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1596 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1596 host target RNA into VGAM1596 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3671] VGAM1597 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1597 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1597 host target RNA into VGAM1597 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3672] It is appreciated that a function of VGR3084 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3084 gene include diagnosis, prevention and treatment of viral infection by Leek Yellow Stripe Potyvirus. Specific functions, and accordingly utilities, of VGR3084 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3084 gene: VGAM1594 host target protein, VGAM1595 host target protein, VGAM1596 host target protein and VGAM1597 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1594, VGAM1595, VGAM1596 and VGAM1597. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic

Record 3085(VGR3085) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3673] VGR3085 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3085 gene was detected is described hereinabove with reference to Figs. 1-9.

[3674] VGR3085 gene encodes VGR3085 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3675] VGR3085 precursor RNA folds spatially, forming VGR3085 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3085 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3085 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[3676] VGR3085 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1598 precursor RNA, VGAM1599 precursor RNA, VGAM1600 precursor RNA, VGAM1601 precursor RNA and VGAM1602 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3677] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1598 RNA, VGAM1599 RNA, VGAM1600 RNA, VGAM1601 RNA and VGAM1602 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3678] VGAM1598 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1598 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1598 host target RNA into VGAM1598 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3679] VGAM1599 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1599 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1599 host target RNA into VGAM1599 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3680] VGAM1600 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1600 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1600 host target RNA into VGAM1600 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3681] VGAM1601 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1601 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1601 host target RNA into VGAM1601 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3682] VGAM1602 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1602 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1602 host target RNA into VGAM1602 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3683] It is appreciated that a function of VGR3085 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3085 gene include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGR3085 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3085 gene: VGAM1598 host target protein, VGAM1599 host target protein, VGAM1600 host target protein, VGAM1601 host target protein and VGAM1602 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1598, VGAM1599, VGAM1600, VGAM1601 and VGAM1602. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3086(VGR3086) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3684] VGR3086 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3086 gene was detected is described hereinabove with reference to Figs. 1-9.

[3685] VGR3086 gene encodes VGR3086 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3686] VGR3086 precursor RNA folds spatially, forming VGR3086 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3086 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3086 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3687] VGR3086 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1603 precursor RNA, VGAM1604 precursor RNA, VGAM1605 precursor RNA, VGAM1606 precursor RNA, VGAM1607 precursor RNA and VGAM1608 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3688] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1603 RNA, VGAM1604 RNA, VGAM1605 RNA, VGAM1606 RNA, VGAM1607 RNA and VGAM1608 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA,

each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3689] VGAM1603 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1603 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1603 host target RNA into VGAM1603 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3690] VGAM1604 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1604 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1604 host target RNA into

VGAM1604 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3691] VGAM1605 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1605 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1605 host target RNA into VGAM1605 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3692] VGAM1606 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1606 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1606 host target RNA into VGAM1606 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3693] VGAM1607 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1607 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1607 host target RNA into VGAM1607 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3694] VGAM1608 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1608 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1608 host target RNA into VGAM1608 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3695] It is appreciated that a function of VGR3086 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3086 gene include diagnosis, prevention and treatment of viral infection by Taura Syndrome Virus. Specific functions, and accordingly utilities, of VGR3086 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3086 gene: VGAM1603 host target protein, VGAM1604 host target protein, VGAM1605 host target protein, VGAM1606 host target protein, VGAM1607 host target protein and VGAM1608 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1603, VGAM1604, VGAM1605, VGAM1606, VGAM1607 and VGAM1608. Fig.

9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3087(VGR3087) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3696] VGR3087 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3087 gene was detected is described hereinabove with reference to Figs. 1-9.

[3697] VGR3087 gene encodes VGR3087 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3698] VGR3087 precursor RNA folds spatially, forming VGR3087 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3087 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3087 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3699] VGR3087 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1609 precursor RNA, VGAM1610 precursor RNA, VGAM1611 precursor RNA, VGAM1612 precursor RNA, VGAM1613 precursor RNA, VGAM1614 precursor RNA, VGAM1615 precursor RNA and VGAM1616 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3700] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1609 RNA, VGAM1610 RNA, VGAM1611 RNA, VGAM1612 RNA, VGAM1613 RNA, VGAM1614 RNA, VGAM1615 RNA and VGAM1616 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3701] VGAM1609 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1609 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1609 host target RNA into VGAM1609 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3702] VGAM1610 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1610 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1610 host target RNA into VGAM1610 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3703] VGAM1611 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1611 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1611 host target RNA into VGAM1611 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3704] VGAM1612 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1612 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1612 host target RNA into VGAM1612 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3705] VGAM1613 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1613 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1613 host target RNA into VGAM1613 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3706] VGAM1614 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1614 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1614 host target RNA into

VGAM1614 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3707] VGAM1615 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1615 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1615 host target RNA into VGAM1615 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3708] VGAM1616 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1616 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1616 host target RNA into VGAM1616 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3709] It is appreciated that a function of VGR3087 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3087 gene include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3087 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3087 gene: VGAM1609 host target protein, VGAM1610 host target protein, VGAM1611 host target protein, VGAM1612 host target protein, VGAM1613 host target protein, VGAM1614 host target protein, VGAM1615 host target protein and VGAM1616 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1609, VGAM1610, VGAM1611, VGAM1612,

VGAM1613, VGAM1614, VGAM1615 and VGAM1616. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3088(VGR3088) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3710] VGR3088 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3088 gene was detected is described hereinabove with reference to Figs. 1-9.

[3711] VGR3088 gene encodes VGR3088 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3712] VGR3088 precursor RNA folds spatially, forming VGR3088 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3088 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3088 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3713] VGR3088 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1617 precursor RNA, VGAM1618 precursor RNA, VGAM1619 precursor RNA, VGAM1620 precursor RNA and VGAM1621 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3714] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1617 RNA, VGAM1618 RNA, VGAM1619 RNA, VGAM1620 RNA and VGAM1621 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3715] VGAM1617 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1617 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1617 host target RNA into VGAM1617 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3716] VGAM1618 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1618 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1618 host target RNA into VGAM1618 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3717] VGAM1619 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1619 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1619 host target RNA into VGAM1619 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3718] VGAM1620 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1620 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1620 host target RNA into VGAM1620 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3719] VGAM1621 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1621 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1621 host target RNA into VGAM1621 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3720] It is appreciated that a function of VGR3088 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3088 gene include diagnosis, prevention and treatment of viral infection by Fowl Adenovirus D. Specific functions, and accordingly utilities, of VGR3088 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3088 gene: VGAM1617 host

target protein, VGAM1618 host target protein, VGAM1619 host target protein, VGAM1620 host target protein and VGAM1621 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1617, VGAM1618, VGAM1619, VGAM1620 and VGAM1621. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3089(VGR3089) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3721] VGR3089 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3089 gene was detected is described hereinabove with reference to Figs. 1-9.

[3722] VGR3089 gene encodes VGR3089 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3723] VGR3089 precursor RNA folds spatially, forming VGR3089 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3089 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3089 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3724] VGR3089 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1622 precursor RNA, VGAM1623 precursor RNA, VGAM1624 precursor RNA, VGAM1625 precursor RNA, VGAM1626 precursor RNA, VGAM1627 precursor RNA, VGAM1628 precursor RNA and VGAM1629 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3725] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1622 RNA, VGAM1623 RNA, VGAM1624 RNA, VGAM1625 RNA, VGAM1626 RNA, VGAM1627 RNA, VGAM1628 RNA and VGAM1629 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3726] VGAM1622 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1622 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1622 host target RNA into VGAM1622 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3727] VGAM1623 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1623 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1623 host target RNA into VGAM1623 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3728] VGAM1624 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1624 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1624 host target RNA into VGAM1624 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3729] VGAM1625 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1625 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1625 host target RNA into VGAM1625 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3730] VGAM1626 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1626 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1626 host target RNA into VGAM1626 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3731] VGAM1627 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1627 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1627 host target RNA into VGAM1627 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3732] VGAM1628 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1628 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1628 host target RNA into VGAM1628 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3733] VGAM1629 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1629 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1629 host target RNA into VGAM1629 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3734] It is appreciated that a function of VGR3089 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3089 gene include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3089 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3089 gene: VGAM1622 host target protein, VGAM1623 host target protein, VGAM1624 host target protein, VGAM1625 host target protein,

VGAM1626 host target protein, VGAM1627 host target protein, VGAM1628 host target protein and VGAM1629 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1622, VGAM1623, VGAM1624, VGAM1625, VGAM1626, VGAM1627, VGAM1628 and VGAM1629. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3090 (VGR3090) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3735] VGR3090 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3090 gene was detected is described hereinabove with reference to Figs. 1-9.

[3736] VGR3090 gene encodes VGR3090 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3737] VGR3090 precursor RNA folds spatially, forming VGR3090 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3090 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3090 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3738] VGR3090 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1630 precursor RNA, VGAM1631 precursor RNA, VGAM1632 precursor RNA, VGAM1633 precursor RNA and VGAM1634 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3739] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1630 RNA, VGAM1631 RNA, VGAM1632 RNA, VGAM1633 RNA and VGAM1634 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3740] VGAM1630 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1630 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1630 host target RNA into VGAM1630 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3741] VGAM1631 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1631 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1631 host target RNA into VGAM1631 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3742] VGAM1632 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1632 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1632 host target RNA into VGAM1632 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3743] VGAM1633 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1633 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1633 host target RNA into VGAM1633 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3744] VGAM1634 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1634 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1634 host target RNA into VGAM1634 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3745] It is appreciated that a function of VGR3090 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3090 gene include

diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3090 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3090 gene: VGAM1630 host target protein, VGAM1631 host target protein, VGAM1632 host target protein, VGAM1633 host target protein and VGAM1634 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1630, VGAM1631, VGAM1632, VGAM1633 and VGAM1634. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3091(VGR3091) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3746] VGR3091 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR3091 gene was detected is described hereinabove with reference to Figs. 1–9.

[3747] VGR3091 gene encodes VGR3091 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3748] VGR3091 precursor RNA folds spatially, forming VGR3091 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3091 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3091 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[3749] VGR3091 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1635 precursor RNA, VGAM1636 precursor RNA, VGAM1637 precursor RNA, VGAM1638 precursor RNA, VGAM1639 precursor RNA and VGAM1640 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3750] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1635 RNA, VGAM1636 RNA, VGAM1637 RNA, VGAM1638 RNA, VGAM1639 RNA and VGAM1640 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3751] VGAM1635 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1635 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1635 host target RNA into VGAM1635 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3752] VGAM1636 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1636 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1636 host target RNA into VGAM1636 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3753] VGAM1637 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1637 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1637 host target RNA into VGAM1637 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3754] VGAM1638 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1638 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1638 host target RNA into VGAM1638 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3755] VGAM1639 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1639 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1639 host target RNA into

VGAM1639 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3756] VGAM1640 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1640 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1640 host target RNA into VGAM1640 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3757] It is appreciated that a function of VGR3091 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3091 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGR3091 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3091 gene: VGAM1635 host
target protein, VGAM1636 host target protein, VGAM1637
host target protein, VGAM1638 host target protein,
VGAM1639 host target protein and VGAM1640 host target
protein, herein schematically represented by VGAM1 HOST
TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN.
The function of these host target genes is elaborated
hereinabove with reference to VGAM1635, VGAM1636,
VGAM1637, VGAM1638, VGAM1639 and VGAM1640. Fig.
9 further provides a conceptual description of novel
bioinformatically detected regulatory viral gene, referred
to here as Viral Genomic Record 3092(VGR3092) viral
gene, which encodes an `operon-like` cluster of novel vi-
ral micro RNA-like genes, each of which in turn modulates
expression of at least one host target gene, the function
and utility of which at least one host target gene is known
in the art.

[3758] VGR3092 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3092 gene was
detected is described hereinabove with reference to Figs.
1-9.

- [3759] VGR3092 gene encodes VGR3092 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [3760] VGR3092 precursor RNA folds spatially, forming VGR3092 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3092 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3092 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [3761] VGR3092 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1641 precursor RNA, VGAM1642 precursor RNA and VGAM1643 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [3762] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1641 RNA, VGAM1642 RNA and VGAM1643 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [3763] VGAM1641 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1641 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1641 host target RNA into VGAM1641 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [3764] VGAM1642 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1642 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1642 host target RNA into VGAM1642 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3765] VGAM1643 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1643 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1643 host target RNA into VGAM1643 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3766] It is appreciated that a function of VGR3092 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3092 gene include diagnosis, prevention and treatment of viral infection by Cell Fusing Agent Virus. Specific functions, and accordingly utilities, of VGR3092 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3092 gene: VGAM1641 host target protein, VGAM1642 host target protein and VGAM1643 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1641, VGAM1642 and VGAM1643. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3093(VGR3093) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3767] VGR3093 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR3093 gene was detected is described hereinabove with reference to Figs. 1-9.

[3768] VGR3093 gene encodes VGR3093 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3769] VGR3093 precursor RNA folds spatially, forming VGR3093 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3093 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3093 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3770] VGR3093 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1644 precursor RNA, VGAM1645 precursor RNA and VGAM1646 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3771] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1644 RNA, VGAM1645 RNA and VGAM1646 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3772] VGAM1644 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1644 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1644 host target RNA into VGAM1644 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3773] VGAM1645 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1645 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1645 host target RNA into VGAM1645 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3774] VGAM1646 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1646 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1646 host target RNA into VGAM1646 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3775] It is appreciated that a function of VGR3093 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3093 gene include diagnosis, prevention and treatment of viral infection by Dengue Virus. Specific functions, and accordingly utilities, of VGR3093 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3093 gene: VGAM1644 host target protein, VGAM1645 host target protein and VGAM1646 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1644, VGAM1645 and VGAM1646. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3094(VGR3094) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3776] VGR3094 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3094 gene was detected is described hereinabove with reference to Figs. 1-9.

[3777] VGR3094 gene encodes VGR3094 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3778] VGR3094 precursor RNA folds spatially, forming VGR3094 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3094 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3094 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3779] VGR3094 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1647 precursor RNA, VGAM1648 precursor RNA, VGAM1649 precursor RNA, VGAM1650

precursor RNA and VGAM1651 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3780] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1647 RNA, VGAM1648 RNA, VGAM1649 RNA, VGAM1650 RNA and VGAM1651 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3781] VGAM1647 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1647 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1647 host target RNA into VGAM1647 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3782] VGAM1648 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1648 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1648 host target RNA into VGAM1648 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3783] VGAM1649 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1649 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1649 host target RNA into

VGAM1649 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3784] VGAM1650 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1650 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1650 host target RNA into VGAM1650 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3785] VGAM1651 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1651 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1651 host target RNA into VGAM1651 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3786] It is appreciated that a function of VGR3094 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3094 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 8. Specific functions, and accordingly utilities, of VGR3094 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3094 gene: VGAM1647 host target protein, VGAM1648 host target protein, VGAM1649 host target protein, VGAM1650 host target protein and VGAM1651 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1647, VGAM1648, VGAM1649, VGAM1650 and VGAM1651. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory vi-

ral gene, referred to here as Viral Genomic Record 3095(VGR3095) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3787] VGR3095 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3095 gene was detected is described hereinabove with reference to Figs. 1-9.

[3788] VGR3095 gene encodes VGR3095 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3789] VGR3095 precursor RNA folds spatially, forming VGR3095 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3095 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3095 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[3790] VGR3095 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1652 precursor RNA, VGAM1653 precursor RNA, VGAM1654 precursor RNA and VGAM1655 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3791] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1652 RNA, VGAM1653 RNA, VGAM1654 RNA and VGAM1655 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3792] VGAM1652 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1652 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1652 host target RNA into VGAM1652 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3793] VGAM1653 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1653 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1653 host target RNA into VGAM1653 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3794] VGAM1654 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1654 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1654 host target RNA into VGAM1654 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3795] VGAM1655 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1655 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1655 host target RNA into VGAM1655 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3796] It is appreciated that a function of VGR3095 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3095 gene include diagnosis, prevention and treatment of viral infection by Yellow Fever Virus. Specific functions, and accordingly utilities, of VGR3095 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3095 gene: VGAM1652 host target protein, VGAM1653 host target protein, VGAM1654 host target protein and VGAM1655 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1652, VGAM1653, VGAM1654 and VGAM1655. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3096(VGR3096) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3797] VGR3096 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR3096 gene was detected is described hereinabove with reference to Figs. 1–9.

[3798] VGR3096 gene encodes VGR3096 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3799] VGR3096 precursor RNA folds spatially, forming VGR3096 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3096 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3096 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[3800] VGR3096 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1656 precursor RNA, VGAM1657 precursor RNA, VGAM1658 precursor RNA, VGAM1659 precursor RNA and VGAM1660 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3801] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1656 RNA, VGAM1657 RNA, VGAM1658 RNA, VGAM1659 RNA and VGAM1660 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3802] VGAM1656 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1656 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1656 host target RNA into VGAM1656 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3803] VGAM1657 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1657 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1657 host target RNA into VGAM1657 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3804] VGAM1658 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1658 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1658 host target RNA into VGAM1658 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3805] VGAM1659 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1659 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1659 host target RNA into VGAM1659 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3806] VGAM1660 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1660 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1660 host target RNA into VGAM1660 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3807] It is appreciated that a function of VGR3096 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3096 gene include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGR3096 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3096 gene: VGAM1656 host target protein, VGAM1657 host target protein, VGAM1658 host target protein, VGAM1659 host target protein and VGAM1660 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1656, VGAM1657, VGAM1658, VGAM1659 and VGAM1660. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3097(VGR3097) viral gene, which encodes an

`operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3808] VGR3097 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3097 gene was detected is described hereinabove with reference to Figs. 1-9.

[3809] VGR3097 gene encodes VGR3097 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3810] VGR3097 precursor RNA folds spatially, forming VGR3097 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3097 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3097 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3811] VGR3097 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1661 precursor RNA, VGAM1662 precursor RNA, VGAM1663 precursor RNA and VGAM1664 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3812] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1661 RNA, VGAM1662 RNA, VGAM1663 RNA and VGAM1664 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3813] VGAM1661 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1661 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1661 host target RNA into VGAM1661 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3814] VGAM1662 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1662 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1662 host target RNA into VGAM1662 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3815] VGAM1663 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1663 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1663 host target RNA into VGAM1663 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3816] VGAM1664 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1664 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1664 host target RNA into VGAM1664 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3817] It is appreciated that a function of VGR3097 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3097 gene include diagnosis, prevention and treatment of viral infection by

Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR3097 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3097 gene: VGAM1661 host target protein, VGAM1662 host target protein, VGAM1663 host target protein and VGAM1664 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1661, VGAM1662, VGAM1663 and VGAM1664. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3098(VGR3098) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3818] VGR3098 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3098 gene was detected is described hereinabove with reference to Figs.

1-9.

[3819] VGR3098 gene encodes VGR3098 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3820] VGR3098 precursor RNA folds spatially, forming VGR3098 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3098 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3098 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3821] VGR3098 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1665 precursor RNA, VGAM1666 precursor RNA and VGAM1667 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[3822] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1665 RNA, VGAM1666 RNA and VGAM1667 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3823] VGAM1665 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1665 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1665 host target RNA into VGAM1665 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3824] VGAM1666 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1666 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1666 host target RNA into VGAM1666 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3825] VGAM1667 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1667 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1667 host target RNA into VGAM1667 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3826] It is appreciated that a function of VGR3098 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3098 gene include diagnosis, prevention and treatment of viral infection by Infectious Spleen and Kidney Necrosis Virus. Specific functions, and accordingly utilities, of VGR3098 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3098 gene: VGAM1665 host target protein, VGAM1666 host target protein and VGAM1667 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1665, VGAM1666 and VGAM1667. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3099(VGR3099) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3827] VGR3099 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3099 gene was detected is described hereinabove with reference to Figs. 1-9.

[3828] VGR3099 gene encodes VGR3099 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3829] VGR3099 precursor RNA folds spatially, forming VGR3099 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3099 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3099 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3830] VGR3099 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1668 precursor RNA, VGAM1669 precursor RNA, VGAM1670 precursor RNA and VGAM1671 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3831] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1668 RNA, VGAM1669 RNA, VGAM1670 RNA and VGAM1671 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3832] VGAM1668 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1668 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1668 host target RNA into VGAM1668 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3833] VGAM1669 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1669 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1669 host target RNA into VGAM1669 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3834] VGAM1670 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1670 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1670 host target RNA into VGAM1670 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3835] VGAM1671 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1671 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1671 host target RNA into VGAM1671 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3836] It is appreciated that a function of VGR3099 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3099 gene include diagnosis, prevention and treatment of viral infection by Human Adenovirus D. Specific functions, and accordingly utilities, of VGR3099 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3099 gene: VGAM1668 host

target protein, VGAM1669 host target protein, VGAM1670 host target protein and VGAM1671 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM1668, VGAM1669, VGAM1670 and VGAM1671. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3100(VGR3100) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3837] VGR3100 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3100 gene was detected is described hereinabove with reference to Figs. 1–9.

[3838] VGR3100 gene encodes VGR3100 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3839] VGR3100 precursor RNA folds spatially, forming VGR3100

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3100 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3100 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3840] VGR3100 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1672 precursor RNA, VGAM1673 precursor RNA and VGAM1674 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3841] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1672 RNA, VGAM1673 RNA and VGAM1674 RNA, herein

schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3842] VGAM1672 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1672 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1672 host target RNA into VGAM1672 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3843] VGAM1673 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1673 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1673 host target RNA into VGAM1673 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3844] VGAM1674 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1674 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1674 host target RNA into VGAM1674 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3845] It is appreciated that a function of VGR3100 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3100 gene include diagnosis, prevention and treatment of viral infection by Tick-borne Encephalitis Virus. Specific functions, and accordingly utilities, of VGR3100 gene correlate with, and

may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3100 gene: VGAM1672 host target protein, VGAM1673 host target protein and VGAM1674 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1672, VGAM1673 and VGAM1674. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3101(VGR3101) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3846] VGR3101 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3101 gene was detected is described hereinabove with reference to Figs. 1-9.

[3847] VGR3101 gene encodes VGR3101 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3848] VGR3101 precursor RNA folds spatially, forming VGR3101 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3101 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3101 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3849] VGR3101 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1675 precursor RNA, VGAM1676 precursor RNA, VGAM1677 precursor RNA, VGAM1678 precursor RNA, VGAM1679 precursor RNA and VGAM1680 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3850] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1675 RNA, VGAM1676 RNA, VGAM1677 RNA, VGAM1678 RNA, VGAM1679 RNA and VGAM1680 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3851] VGAM1675 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1675 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1675 host target RNA into VGAM1675 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3852] VGAM1676 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1676 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1676 host target RNA into VGAM1676 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3853] VGAM1677 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1677 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1677 host target RNA into VGAM1677 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3854] VGAM1678 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1678 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1678 host target RNA into VGAM1678 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3855] VGAM1679 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1679 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1679 host target RNA into VGAM1679 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3856] VGAM1680 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1680 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1680 host target RNA into VGAM1680 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3857] It is appreciated that a function of VGR3101 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3101 gene include diagnosis, prevention and treatment of viral infection by Viral Hemorrhagic Septicemia Virus. Specific functions, and accordingly utilities, of VGR3101 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3101 gene: VGAM1675 host target protein, VGAM1676 host target protein, VGAM1677 host target protein, VGAM1678 host target

protein, VGAM1679 host target protein and VGAM1680 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1675, VGAM1676, VGAM1677, VGAM1678, VGAM1679 and VGAM1680. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3102(VGR3102) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3858] VGR3102 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3102 gene was detected is described hereinabove with reference to Figs. 1-9.

[3859] VGR3102 gene encodes VGR3102 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3860] VGR3102 precursor RNA folds spatially, forming VGR3102

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3102 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3102 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3861] VGR3102 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1681 precursor RNA, VGAM1682 precursor RNA, VGAM1683 precursor RNA, VGAM1684 precursor RNA, VGAM1685 precursor RNA and VGAM1686 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3862] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1681

RNA, VGAM1682 RNA, VGAM1683 RNA, VGAM1684 RNA, VGAM1685 RNA and VGAM1686 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3863] VGAM1681 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1681 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1681 host target RNA into VGAM1681 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3864] VGAM1682 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1682 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1682 host target RNA into VGAM1682 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3865] VGAM1683 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1683 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1683 host target RNA into VGAM1683 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3866] VGAM1684 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1684 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1684 host target RNA into VGAM1684 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3867] VGAM1685 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1685 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1685 host target RNA into VGAM1685 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3868] VGAM1686 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1686 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1686 host target RNA into VGAM1686 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3869] It is appreciated that a function of VGR3102 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3102 gene include diagnosis, prevention and treatment of viral infection by Vesicular Stomatitis Indiana Virus. Specific functions, and accordingly utilities, of VGR3102 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3102 gene: VGAM1681 host target protein, VGAM1682 host target protein, VGAM1683 host target protein, VGAM1684 host target protein, VGAM1685 host target protein and VGAM1686 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1681, VGAM1682, VGAM1683, VGAM1684, VGAM1685 and VGAM1686. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3103(VGR3103) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3870] VGR3103 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3103 gene was detected is described hereinabove with reference to Figs. 1-9.

[3871] VGR3103 gene encodes VGR3103 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3872] VGR3103 precursor RNA folds spatially, forming VGR3103 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3103 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3103 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3873] VGR3103 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1687 precursor RNA, VGAM1688 precursor RNA and VGAM1689 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3874] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1687 RNA, VGAM1688 RNA and VGAM1689 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3875] VGAM1687 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1687 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1687 host target RNA into VGAM1687 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3876] VGAM1688 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1688 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1688 host target RNA into VGAM1688 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3877] VGAM1689 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1689 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1689 host target RNA into VGAM1689 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3878] It is appreciated that a function of VGR3103 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3103 gene include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3103 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3103 gene: VGAM1687

host target protein, VGAM1688 host target protein and VGAM1689 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1687, VGAM1688 and VGAM1689. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3104(VGR3104) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3879] VGR3104 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3104 gene was detected is described hereinabove with reference to Figs. 1-9.

[3880] VGR3104 gene encodes VGR3104 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3881] VGR3104 precursor RNA folds spatially, forming VGR3104

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3104 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3104 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3882] VGR3104 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1690 precursor RNA, VGAM1691 precursor RNA, VGAM1692 precursor RNA, VGAM1693 precursor RNA, VGAM1694 precursor RNA, VGAM1695 precursor RNA, VGAM1696 precursor RNA and VGAM1697 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3883] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1690 RNA, VGAM1691 RNA, VGAM1692 RNA, VGAM1693 RNA, VGAM1694 RNA, VGAM1695 RNA, VGAM1696 RNA and VGAM1697 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3884] VGAM1690 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1690 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1690 host target RNA into VGAM1690 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3885] VGAM1691 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1691 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1691 host target RNA into VGAM1691 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3886] VGAM1692 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1692 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1692 host target RNA into VGAM1692 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3887] VGAM1693 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1693 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1693 host target RNA into VGAM1693 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3888] VGAM1694 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1694 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1694 host target RNA into VGAM1694 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3889] VGAM1695 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1695 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1695 host target RNA into VGAM1695 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3890] VGAM1696 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1696 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1696 host target RNA into VGAM1696 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3891] VGAM1697 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1697 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1697 host target RNA into VGAM1697 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3892] It is appreciated that a function of VGR3104 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3104 gene include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGR3104 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3104 gene: VGAM1690 host target protein, VGAM1691 host target protein, VGAM1692 host target protein, VGAM1693 host target protein, VGAM1694 host target protein, VGAM1695 host

target protein, VGAM1696 host target protein and VGAM1697 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1690, VGAM1691, VGAM1692, VGAM1693, VGAM1694, VGAM1695, VGAM1696 and VGAM1697. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3105(VGR3105) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3893] VGR3105 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3105 gene was detected is described hereinabove with reference to Figs. 1-9.

[3894] VGR3105 gene encodes VGR3105 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3895] VGR3105 precursor RNA folds spatially, forming VGR3105 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3105 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3105 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3896] VGR3105 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1698 precursor RNA, VGAM1699 precursor RNA, VGAM1700 precursor RNA, VGAM1701 precursor RNA, VGAM1702 precursor RNA, VGAM1703 precursor RNA, VGAM1704 precursor RNA and VGAM1705 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3897] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1698 RNA, VGAM1699 RNA, VGAM1700 RNA, VGAM1701 RNA, VGAM1702 RNA, VGAM1703 RNA, VGAM1704 RNA and VGAM1705 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3898] VGAM1698 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1698 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1698 host target RNA into VGAM1698 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3899] VGAM1699 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1699 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1699 host target RNA into VGAM1699 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3900] VGAM1700 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1700 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1700 host target RNA into VGAM1700 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3901] VGAM1701 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1701 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1701 host target RNA into VGAM1701 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3902] VGAM1702 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1702 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1702 host target RNA into VGAM1702 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3903] VGAM1703 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1703 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1703 host target RNA into VGAM1703 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3904] VGAM1704 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1704 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1704 host target RNA into VGAM1704 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3905] VGAM1705 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1705 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1705 host target RNA into VGAM1705 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3906] It is appreciated that a function of VGR3105 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3105 gene include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGR3105 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3105 gene: VGAM1698 host target protein, VGAM1699 host target protein, VGAM1700 host target protein, VGAM1701 host target

protein, VGAM1702 host target protein, VGAM1703 host target protein, VGAM1704 host target protein and VGAM1705 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1698, VGAM1699, VGAM1700, VGAM1701, VGAM1702, VGAM1703, VGAM1704 and VGAM1705. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3106(VGR3106) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3907] VGR3106 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3106 gene was detected is described hereinabove with reference to Figs. 1-9.

[3908] VGR3106 gene encodes VGR3106 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[3909] VGR3106 precursor RNA folds spatially, forming VGR3106 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3106 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3106 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3910] VGR3106 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1706 precursor RNA and VGAM1707 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3911] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1706

RNA and VGAM1707 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3912] VGAM1706 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1706 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1706 host target RNA into VGAM1706 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3913] VGAM1707 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1707 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1707 host target RNA into VGAM1707 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3914] It is appreciated that a function of VGR3106 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3106 gene include diagnosis, prevention and treatment of viral infection by Ectocarpus Siliculosus Virus. Specific functions, and accordingly utilities, of VGR3106 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3106 gene: VGAM1706 host target protein and VGAM1707 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1706 and VGAM1707. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3107(VGR3107) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3915] VGR3107 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3107 gene was detected is described hereinabove with reference to Figs. 1-9.

[3916] VGR3107 gene encodes VGR3107 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3917] VGR3107 precursor RNA folds spatially, forming VGR3107 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3107 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3107 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3918] VGR3107 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1709 precursor RNA, VGAM1710 precursor RNA and VGAM1711 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3919] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1709 RNA, VGAM1710 RNA and VGAM1711 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3920] VGAM1709 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1709 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1709 host target RNA into VGAM1709 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3921] VGAM1710 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1710 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1710 host target RNA into VGAM1710 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3922] VGAM1711 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1711 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1711 host target RNA into VGAM1711 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3923] It is appreciated that a function of VGR3107 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3107 gene include diagnosis, prevention and treatment of viral infection by Semliki Forest Virus. Specific functions, and accordingly utilities, of VGR3107 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3107 gene: VGAM1709 host target protein, VGAM1710 host target protein and VGAM1711 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1709, VGAM1710 and VGAM1711. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 3108(VGR3108) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3924] VGR3108 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3108 gene was detected is described hereinabove with reference to Figs. 1-9.

[3925] VGR3108 gene encodes VGR3108 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3926] VGR3108 precursor RNA folds spatially, forming VGR3108 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3108 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3108 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3927] VGR3108 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1712 precursor RNA, VGAM1713 precursor RNA, VGAM1714 precursor RNA, VGAM1715 precursor RNA and VGAM1716 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3928] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1712 RNA, VGAM1713 RNA, VGAM1714 RNA, VGAM1715 RNA and VGAM1716 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3929] VGAM1712 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1712 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1712 host target RNA into VGAM1712 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3930] VGAM1713 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1713 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1713 host target RNA into VGAM1713 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3931] VGAM1714 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1714 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1714 host target RNA into VGAM1714 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3932] VGAM1715 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1715 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1715 host target RNA into VGAM1715 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3933] VGAM1716 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1716 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1716 host target RNA into VGAM1716 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3934] It is appreciated that a function of VGR3108 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3108 gene include diagnosis, prevention and treatment of viral infection by Sindbis Virus. Specific functions, and accordingly utilities, of VGR3108 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3108 gene: VGAM1712 host target protein, VGAM1713 host target protein, VGAM1714 host target protein, VGAM1715 host target protein and VGAM1716

host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1712, VGAM1713, VGAM1714, VGAM1715 and VGAM1716. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3109(VGR3109) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3935] VGR3109 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3109 gene was detected is described hereinabove with reference to Figs. 1-9.

[3936] VGR3109 gene encodes VGR3109 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3937] VGR3109 precursor RNA folds spatially, forming VGR3109 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3109 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3109 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3938] VGR3109 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1717 precursor RNA and VGAM1718 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3939] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1717 RNA and VGAM1718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3940] VGAM1717 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1717 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1717 host target RNA into VGAM1717 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3941] VGAM1718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1718 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1718 host target RNA into VGAM1718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3942] It is appreciated that a function of VGR3109 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3109 gene include diagnosis, prevention and treatment of viral infection by Mollusum Contagiosum Virus. Specific functions, and accordingly utilities, of VGR3109 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3109 gene: VGAM1717 host target protein and VGAM1718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1717 and VGAM1718. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3110(VGR3110) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in

the art.

[3943] VGR3110 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3110 gene was detected is described hereinabove with reference to Figs. 1-9.

[3944] VGR3110 gene encodes VGR3110 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3945] VGR3110 precursor RNA folds spatially, forming VGR3110 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3110 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3110 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3946] VGR3110 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1719 precursor RNA and

VGAM1720 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3947] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1719 RNA and VGAM1720 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3948] VGAM1719 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1719 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1719 host target RNA into VGAM1719 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3949] VGAM1720 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1720 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1720 host target RNA into VGAM1720 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3950] It is appreciated that a function of VGR3110 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3110 gene include diagnosis, prevention and treatment of viral infection by Rat Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3110 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3110 gene: VGAM1719 host target protein and VGAM1720 host target protein, herein

schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1719 and VGAM1720. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3111(VGR3111) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3951] VGR3111 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3111 gene was detected is described hereinabove with reference to Figs. 1-9.

[3952] VGR3111 gene encodes VGR3111 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3953] VGR3111 precursor RNA folds spatially, forming VGR3111 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3111 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3111 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3954] VGR3111 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1721 precursor RNA, VGAM1722 precursor RNA and VGAM1723 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3955] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1721 RNA, VGAM1722 RNA and VGAM1723 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM

RNA of Fig. 1.

[3956] VGAM1721 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1721 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1721 host target RNA into VGAM1721 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3957] VGAM1722 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1722 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1722 host target RNA into VGAM1722 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3958] VGAM1723 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1723 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1723 host target RNA into VGAM1723 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3959] It is appreciated that a function of VGR3111 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3111 gene include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGR3111 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3111 gene: VGAM1721 host target protein, VGAM1722 host target protein and VGAM1723 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1721, VGAM1722 and VGAM1723. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3112(VGR3112) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3960] VGR3112 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3112 gene was detected is described hereinabove with reference to Figs. 1-9.

[3961] VGR3112 gene encodes VGR3112 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3962] VGR3112 precursor RNA folds spatially, forming VGR3112 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3112 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3112 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3963] VGR3112 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1724 precursor RNA, VGAM1725 precursor RNA, VGAM1726 precursor RNA, VGAM1727 precursor RNA, VGAM1728 precursor RNA, VGAM1729 precursor RNA and VGAM1730 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3964] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1724 RNA, VGAM1725 RNA, VGAM1726 RNA, VGAM1727 RNA, VGAM1728 RNA, VGAM1729 RNA and VGAM1730 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3965] VGAM1724 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1724 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1724 host target RNA into VGAM1724 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3966] VGAM1725 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1725 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1725 host target RNA into VGAM1725 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3967] VGAM1726 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1726 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1726 host target RNA into VGAM1726 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3968] VGAM1727 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1727 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1727 host target RNA into VGAM1727 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3969] VGAM1728 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1728 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1728 host target RNA into VGAM1728 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3970] VGAM1729 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1729 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1729 host target RNA into VGAM1729 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3971] VGAM1730 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1730 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1730 host target RNA into VGAM1730 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3972] It is appreciated that a function of VGR3112 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3112 gene include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGR3112 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3112 gene: VGAM1724 host target protein, VGAM1725 host target protein, VGAM1726 host target protein, VGAM1727 host target protein, VGAM1728 host target protein, VGAM1729 host target protein and VGAM1730 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1724, VGAM1725, VGAM1726, VGAM1727, VGAM1728, VGAM1729 and VGAM1730. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3113(VGR3113) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3973] VGR3113 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3113 gene was detected is described hereinabove with reference to Figs. 1-9.

[3974] VGR3113 gene encodes VGR3113 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3975] VGR3113 precursor RNA folds spatially, forming VGR3113 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3113 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3113 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3976] VGR3113 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM

precursor RNAs, VGAM1731 precursor RNA and VGAM1732 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3977] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1731 RNA and VGAM1732 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3978] VGAM1731 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1731 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1731 host target RNA into VGAM1731 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3979] VGAM1732 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1732 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1732 host target RNA into VGAM1732 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3980] It is appreciated that a function of VGR3113 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3113 gene include diagnosis, prevention and treatment of viral infection by Rabies Virus. Specific functions, and accordingly utilities, of VGR3113 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3113 gene: VGAM1731 host target protein

and VGAM1732 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1731 and VGAM1732. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3114(VGR3114) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3981] VGR3114 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3114 gene was detected is described hereinabove with reference to Figs. 1-9.

[3982] VGR3114 gene encodes VGR3114 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3983] VGR3114 precursor RNA folds spatially, forming VGR3114 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3114 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3114 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3984] VGR3114 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1733 precursor RNA, VGAM1734 precursor RNA, VGAM1735 precursor RNA, VGAM1736 precursor RNA, VGAM1737 precursor RNA, VGAM1738 precursor RNA, VGAM1739 precursor RNA and VGAM1740 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3985] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1733 RNA, VGAM1734 RNA, VGAM1735 RNA, VGAM1736 RNA,

VGAM1737 RNA, VGAM1738 RNA, VGAM1739 RNA and VGAM1740 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[3986] VGAM1733 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1733 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1733 host target RNA into VGAM1733 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3987] VGAM1734 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1734 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1734 host target RNA into VGAM1734 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3988] VGAM1735 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1735 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1735 host target RNA into VGAM1735 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3989] VGAM1736 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1736 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1736 host target RNA into VGAM1736 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3990] VGAM1737 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1737 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1737 host target RNA into VGAM1737 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3991] VGAM1738 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1738 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1738 host target RNA into VGAM1738 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3992] VGAM1739 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1739 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1739 host target RNA into VGAM1739 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3993] VGAM1740 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1740 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1740 host target RNA into VGAM1740 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[3994] It is appreciated that a function of VGR3114 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3114 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3114 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3114 gene: VGAM1733 host target protein, VGAM1734 host target protein, VGAM1735 host target protein, VGAM1736 host target protein, VGAM1737 host target protein, VGAM1738 host target protein, VGAM1739 host target protein and VGAM1740 host target protein, herein schematically represented by

VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1733, VGAM1734, VGAM1735, VGAM1736, VGAM1737, VGAM1738, VGAM1739 and VGAM1740. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3115 (VGR3115) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[3995] VGR3115 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3115 gene was detected is described hereinabove with reference to Figs. 1-9.

[3996] VGR3115 gene encodes VGR3115 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[3997] VGR3115 precursor RNA folds spatially, forming VGR3115 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3115 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3115 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[3998] VGR3115 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1741 precursor RNA, VGAM1742 precursor RNA, VGAM1743 precursor RNA, VGAM1744 precursor RNA, VGAM1745 precursor RNA and VGAM1746 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[3999] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1741 RNA, VGAM1742 RNA, VGAM1743 RNA, VGAM1744 RNA, VGAM1745 RNA and VGAM1746 RNA, herein schemati-

cally represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4000] VGAM1741 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1741 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1741 host target RNA into VGAM1741 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4001] VGAM1742 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1742 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1742 host target RNA into VGAM1742 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4002] VGAM1743 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1743 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1743 host target RNA into VGAM1743 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4003] VGAM1744 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1744 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1744 host target RNA into VGAM1744 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4004] VGAM1745 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1745 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1745 host target RNA into VGAM1745 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4005] VGAM1746 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1746 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1746 host target RNA into VGAM1746 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4006] It is appreciated that a function of VGR3115 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3115 gene include diagnosis, prevention and treatment of viral infection by Cercopithecine Herpesvirus 7. Specific functions, and accordingly utilities, of VGR3115 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3115 gene: VGAM1741 host target protein, VGAM1742 host target protein, VGAM1743 host target protein, VGAM1744 host target protein, VGAM1745 host target protein and VGAM1746 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1741,

VGAM1742, VGAM1743, VGAM1744, VGAM1745 and VGAM1746. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3116 (VGR3116) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4007] VGR3116 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3116 gene was detected is described hereinabove with reference to Figs. 1-9.

[4008] VGR3116 gene encodes VGR3116 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4009] VGR3116 precursor RNA folds spatially, forming VGR3116 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3116 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3116 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4010] VGR3116 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1747 precursor RNA, VGAM1748 precursor RNA, VGAM1749 precursor RNA, VGAM1750 precursor RNA, VGAM1751 precursor RNA, VGAM1752 precursor RNA, VGAM1753 precursor RNA and VGAM1754 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4011] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1747 RNA, VGAM1748 RNA, VGAM1749 RNA, VGAM1750 RNA, VGAM1751 RNA, VGAM1752 RNA, VGAM1753 RNA and VGAM1754 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[4012] VGAM1747 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1747 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1747 host target RNA into VGAM1747 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4013] VGAM1748 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1748 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1748 host target RNA into VGAM1748 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4014] VGAM1749 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1749 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1749 host target RNA into VGAM1749 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4015] VGAM1750 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1750 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1750 host target RNA into

VGAM1750 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4016] VGAM1751 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1751 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1751 host target RNA into VGAM1751 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4017] VGAM1752 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1752 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1752 host target RNA into VGAM1752 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4018] VGAM1753 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1753 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1753 host target RNA into VGAM1753 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4019] VGAM1754 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1754 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1754 host target RNA into VGAM1754 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4020] It is appreciated that a function of VGR3116 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3116 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3116 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3116 gene: VGAM1747 host target protein, VGAM1748 host target protein, VGAM1749 host target protein, VGAM1750 host target protein, VGAM1751 host target protein, VGAM1752 host target protein, VGAM1753 host target protein and VGAM1754 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1747,

VGAM1748, VGAM1749, VGAM1750, VGAM1751, VGAM1752, VGAM1753 and VGAM1754. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3117 (VGR3117) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4021] VGR3117 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3117 gene was detected is described hereinabove with reference to Figs. 1-9.

[4022] VGR3117 gene encodes VGR3117 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4023] VGR3117 precursor RNA folds spatially, forming VGR3117 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3117 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3117 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4024] VGR3117 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM1755 precursor RNA, VGAM1756 precursor RNA, VGAM1757 precursor RNA and VGAM1758 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4025] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1755 RNA, VGAM1756 RNA, VGAM1757 RNA and VGAM1758 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4026] VGAM1755 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1755 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1755 host target RNA into VGAM1755 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4027] VGAM1756 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1756 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1756 host target RNA into VGAM1756 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4028] VGAM1757 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1757 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1757 host target RNA into VGAM1757 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4029] VGAM1758 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1758 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1758 host target RNA into VGAM1758 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4030] It is appreciated that a function of VGR3117 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3117 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3117 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3117 gene: VGAM1755 host target protein, VGAM1756 host target protein, VGAM1757 host target protein and VGAM1758 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1755, VGAM1756, VGAM1757 and VGAM1758. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3118(VGR3118) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least

one host target gene is known in the art.

[4031] VGR3118 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3118 gene was detected is described hereinabove with reference to Figs. 1-9.

[4032] VGR3118 gene encodes VGR3118 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4033] VGR3118 precursor RNA folds spatially, forming VGR3118 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3118 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3118 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4034] VGR3118 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1759 precursor RNA, VGAM1760

precursor RNA, VGAM1761 precursor RNA, VGAM1762 precursor RNA, VGAM1763 precursor RNA, VGAM1764 precursor RNA, VGAM1765 precursor RNA and VGAM1766 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4035] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1759 RNA, VGAM1760 RNA, VGAM1761 RNA, VGAM1762 RNA, VGAM1763 RNA, VGAM1764 RNA, VGAM1765 RNA and VGAM1766 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4036] VGAM1759 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1759 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1759 host target RNA into VGAM1759 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4037] VGAM1760 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1760 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1760 host target RNA into VGAM1760 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4038] VGAM1761 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1761 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1761 host target RNA into VGAM1761 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4039] VGAM1762 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1762 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1762 host target RNA into VGAM1762 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4040] VGAM1763 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1763 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1763 host target RNA into VGAM1763 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4041] VGAM1764 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1764 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1764 host target RNA into VGAM1764 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4042] VGAM1765 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1765 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1765 host target RNA into VGAM1765 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4043] VGAM1766 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1766 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1766 host target RNA into VGAM1766 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4044] It is appreciated that a function of VGR3118 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3118 gene include diagnosis, prevention and treatment of viral infection by Bovine Viral Diarrhea Virus Genotype 2 (BVDV-2). Specific functions, and accordingly utilities, of VGR3118 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3118 gene: VGAM1759 host target protein, VGAM1760 host target protein, VGAM1761 host target protein, VGAM1762 host target protein, VGAM1763 host target protein, VGAM1764 host target protein, VGAM1765 host target protein and VGAM1766 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1759, VGAM1760, VGAM1761, VGAM1762, VGAM1763, VGAM1764, VGAM1765 and VGAM1766. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3119(VGR3119) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function

and utility of which at least one host target gene is known in the art.

[4045] VGR3119 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3119 gene was detected is described hereinabove with reference to Figs. 1-9.

[4046] VGR3119 gene encodes VGR3119 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4047] VGR3119 precursor RNA folds spatially, forming VGR3119 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3119 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3119 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4048] VGR3119 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM

precursor RNAs, VGAM1767 precursor RNA, VGAM1768 precursor RNA, VGAM1769 precursor RNA and VGAM1770 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4049] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1767 RNA, VGAM1768 RNA, VGAM1769 RNA and VGAM1770 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4050] VGAM1767 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1767 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1767 host target RNA into

VGAM1767 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4051] VGAM1768 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1768 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1768 host target RNA into VGAM1768 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4052] VGAM1769 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1769 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1769 host target RNA into VGAM1769 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4053] VGAM1770 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1770 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1770 host target RNA into VGAM1770 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4054] It is appreciated that a function of VGR3119 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3119 gene include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGR3119 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3119 gene: VGAM1767 host target protein, VGAM1768 host target protein, VGAM1769 host target protein and VGAM1770 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1767, VGAM1768, VGAM1769 and VGAM1770. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3120(VGR3120) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4055] VGR3120 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3120 gene was detected is described hereinabove with reference to Figs. 1-9.

[4056] VGR3120 gene encodes VGR3120 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4057] VGR3120 precursor RNA folds spatially, forming VGR3120 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3120 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3120 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4058] VGR3120 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1771 precursor RNA and VGAM1772 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4059] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1771 RNA and VGAM1772 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4060] VGAM1771 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1771 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1771 host target RNA into VGAM1771 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4061] VGAM1772 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1772 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1772 host target RNA into VGAM1772 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4062] It is appreciated that a function of VGR3120 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3120 gene include diagnosis, prevention and treatment of viral infection by Pestivirus Type 1. Specific functions, and accordingly utilities, of VGR3120 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3120 gene: VGAM1771 host target protein and VGAM1772 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1771 and VGAM1772. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3121(VGR3121) viral gene, which

encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4063] VGR3121 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3121 gene was detected is described hereinabove with reference to Figs. 1-9.

[4064] VGR3121 gene encodes VGR3121 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4065] VGR3121 precursor RNA folds spatially, forming VGR3121 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3121 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3121 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[4066] VGR3121 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1773 precursor RNA, VGAM1774 precursor RNA, VGAM1775 precursor RNA, VGAM1776 precursor RNA, VGAM1777 precursor RNA, VGAM1778 precursor RNA, VGAM1779 precursor RNA and VGAM1780 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4067] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1773 RNA, VGAM1774 RNA, VGAM1775 RNA, VGAM1776 RNA, VGAM1777 RNA, VGAM1778 RNA, VGAM1779 RNA and VGAM1780 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4068] VGAM1773 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1773 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1773 host target RNA into VGAM1773 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4069] VGAM1774 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1774 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1774 host target RNA into VGAM1774 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4070] VGAM1775 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1775 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1775 host target RNA into VGAM1775 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4071] VGAM1776 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1776 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1776 host target RNA into VGAM1776 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4072] VGAM1777 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1777 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1777 host target RNA into VGAM1777 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4073] VGAM1778 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1778 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1778 host target RNA into VGAM1778 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4074] VGAM1779 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1779 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1779 host target RNA into VGAM1779 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4075] VGAM1780 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1780 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1780 host target RNA into VGAM1780 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4076] It is appreciated that a function of VGR3121 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3121 gene include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and accordingly utilities, of VGR3121 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3121 gene: VGAM1773 host target protein, VGAM1774 host target protein, VGAM1775 host target protein, VGAM1776 host target protein, VGAM1777 host target protein, VGAM1778 host target protein, VGAM1779 host target protein and VGAM1780 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1773, VGAM1774, VGAM1775, VGAM1776, VGAM1777, VGAM1778, VGAM1779 and VGAM1780. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred

to here as Viral Genomic Record 3122(VGR3122) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4077] VGR3122 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3122 gene was detected is described hereinabove with reference to Figs. 1-9.

[4078] VGR3122 gene encodes VGR3122 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4079] VGR3122 precursor RNA folds spatially, forming VGR3122 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3122 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3122 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4080] VGR3122 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1781 precursor RNA and VGAM1782 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4081] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1781 RNA and VGAM1782 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4082] VGAM1781 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1781 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1781 host target RNA into VGAM1781 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4083] VGAM1782 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1782 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1782 host target RNA into VGAM1782 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4084] It is appreciated that a function of VGR3122 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3122 gene include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 1. Specific functions, and ac-

cordingly utilities, of VGR3122 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3122 gene: VGAM1781 host target protein and VGAM1782 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1781 and VGAM1782. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3123(VGR3123) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4085] VGR3123 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3123 gene was detected is described hereinabove with reference to Figs. 1-9.

[4086] VGR3123 gene encodes VGR3123 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4087] VGR3123 precursor RNA folds spatially, forming VGR3123 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3123 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3123 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4088] VGR3123 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1783 precursor RNA, VGAM1784 precursor RNA, VGAM1785 precursor RNA, VGAM1786 precursor RNA, VGAM1787 precursor RNA, VGAM1788 precursor RNA and VGAM1789 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[4089] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1783 RNA, VGAM1784 RNA, VGAM1785 RNA, VGAM1786 RNA, VGAM1787 RNA, VGAM1788 RNA and VGAM1789 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4090] VGAM1783 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1783 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1783 host target RNA into VGAM1783 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4091] VGAM1784 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1784 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1784 host target RNA into VGAM1784 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4092] VGAM1785 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1785 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1785 host target RNA into VGAM1785 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4093] VGAM1786 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1786 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1786 host target RNA into VGAM1786 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4094] VGAM1787 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1787 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1787 host target RNA into VGAM1787 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4095] VGAM1788 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1788 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1788 host target RNA into VGAM1788 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4096] VGAM1789 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1789 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1789 host target RNA into VGAM1789 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4097] It is appreciated that a function of VGR3123 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3123 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3123 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3123 gene: VGAM1783 host target protein, VGAM1784 host target protein, VGAM1785 host target protein, VGAM1786 host target protein, VGAM1787 host target protein, VGAM1788 host target protein and VGAM1789 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1783, VGAM1784, VGAM1785, VGAM1786, VGAM1787, VGAM1788 and VGAM1789. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3124(VGR3124) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4098] VGR3124 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3124 gene was detected is described hereinabove with reference to Figs. 1-9.

- [4099] VGR3124 gene encodes VGR3124 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [4100] VGR3124 precursor RNA folds spatially, forming VGR3124 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3124 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3124 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [4101] VGR3124 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1790 precursor RNA, VGAM1791 precursor RNA, VGAM1792 precursor RNA, VGAM1793 precursor RNA, VGAM1794 precursor RNA, VGAM1795 precursor RNA and VGAM1796 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4102] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1790 RNA, VGAM1791 RNA, VGAM1792 RNA, VGAM1793 RNA, VGAM1794 RNA, VGAM1795 RNA and VGAM1796 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4103] VGAM1790 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1790 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1790 host target RNA into VGAM1790 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4104] VGAM1791 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1791 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1791 host target RNA into VGAM1791 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4105] VGAM1792 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1792 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1792 host target RNA into VGAM1792 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4106] VGAM1793 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1793 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1793 host target RNA into VGAM1793 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4107] VGAM1794 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1794 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1794 host target RNA into VGAM1794 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4108] VGAM1795 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1795 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1795 host target RNA into VGAM1795 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4109] VGAM1796 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1796 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1796 host target RNA into VGAM1796 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4110] It is appreciated that a function of VGR3124 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3124 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3124 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3124 gene: VGAM1790 host target protein, VGAM1791 host target protein, VGAM1792 host target protein, VGAM1793 host target protein, VGAM1794 host target protein, VGAM1795 host target protein and VGAM1796 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1790, VGAM1791, VGAM1792, VGAM1793, VGAM1794, VGAM1795 and VGAM1796. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred

to here as Viral Genomic Record 3125(VGR3125) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4111] VGR3125 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3125 gene was detected is described hereinabove with reference to Figs. 1-9.

[4112] VGR3125 gene encodes VGR3125 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4113] VGR3125 precursor RNA folds spatially, forming VGR3125 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3125 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3125 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4114] VGR3125 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1797 precursor RNA and VGAM1798 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4115] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1797 RNA and VGAM1798 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4116] VGAM1797 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1797 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1797 host target RNA into VGAM1797 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4117] VGAM1798 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1798 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1798 host target RNA into VGAM1798 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4118] It is appreciated that a function of VGR3125 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3125 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accord-

ingly utilities, of VGR3125 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3125 gene: VGAM1797 host target protein and VGAM1798 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1797 and VGAM1798. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3126(VGR3126) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4119] VGR3126 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3126 gene was detected is described hereinabove with reference to Figs. 1-9.

[4120] VGR3126 gene encodes VGR3126 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4121] VGR3126 precursor RNA folds spatially, forming VGR3126 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3126 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3126 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4122] VGR3126 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1799 precursor RNA, VGAM1800 precursor RNA, VGAM1801 precursor RNA, VGAM1802 precursor RNA, VGAM1803 precursor RNA, VGAM1804 precursor RNA, VGAM1805 precursor RNA and VGAM1806 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM

FOLDED PRECURSOR RNA of Fig. 1.

[4123] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1799 RNA, VGAM1800 RNA, VGAM1801 RNA, VGAM1802 RNA, VGAM1803 RNA, VGAM1804 RNA, VGAM1805 RNA and VGAM1806 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4124] VGAM1799 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1799 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1799 host target RNA into VGAM1799 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4125] VGAM1800 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1800 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1800 host target RNA into VGAM1800 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4126] VGAM1801 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1801 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1801 host target RNA into VGAM1801 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4127] VGAM1802 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1802 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1802 host target RNA into VGAM1802 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4128] VGAM1803 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1803 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1803 host target RNA into VGAM1803 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4129] VGAM1804 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1804 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1804 host target RNA into VGAM1804 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4130] VGAM1805 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1805 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1805 host target RNA into VGAM1805 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4131] VGAM1806 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1806 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1806 host target RNA into VGAM1806 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4132] It is appreciated that a function of VGR3126 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3126 gene include diagnosis, prevention and treatment of viral infection by Tupaia Herpesvirus. Specific functions, and accordingly utilities, of VGR3126 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3126 gene: VGAM1799 host

target protein, VGAM1800 host target protein, VGAM1801 host target protein, VGAM1802 host target protein, VGAM1803 host target protein, VGAM1804 host target protein, VGAM1805 host target protein and VGAM1806 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1799, VGAM1800, VGAM1801, VGAM1802, VGAM1803, VGAM1804, VGAM1805 and VGAM1806. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3127 (VGR3127) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4133] VGR3127 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3127 gene was detected is described hereinabove with reference to Figs. 1-9.

[4134] VGR3127 gene encodes VGR3127 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4135] VGR3127 precursor RNA folds spatially, forming VGR3127 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3127 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3127 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4136] VGR3127 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1807 precursor RNA, VGAM1808 precursor RNA and VGAM1809 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4137] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1807 RNA, VGAM1808 RNA and VGAM1809 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4138] VGAM1807 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1807 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1807 host target RNA into VGAM1807 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4139] VGAM1808 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1808 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1808 host target RNA into VGAM1808 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4140] VGAM1809 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1809 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1809 host target RNA into VGAM1809 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4141] It is appreciated that a function of VGR3127 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3127 gene include

diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3127 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3127 gene: VGAM1807 host target protein, VGAM1808 host target protein and VGAM1809 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1807, VGAM1808 and VGAM1809. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3128(VGR3128) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4142] VGR3128 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3128 gene was

detected is described hereinabove with reference to Figs. 1-9.

[4143] VGR3128 gene encodes VGR3128 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4144] VGR3128 precursor RNA folds spatially, forming VGR3128 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3128 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3128 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4145] VGR3128 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1810 precursor RNA, VGAM1811 precursor RNA, VGAM1812 precursor RNA, VGAM1813 precursor RNA, VGAM1814 precursor RNA and VGAM1815 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4146] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1810 RNA, VGAM1811 RNA, VGAM1812 RNA, VGAM1813 RNA, VGAM1814 RNA and VGAM1815 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4147] VGAM1810 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1810 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1810 host target RNA into VGAM1810 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4148] VGAM1811 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1811 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1811 host target RNA into VGAM1811 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4149] VGAM1812 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1812 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1812 host target RNA into VGAM1812 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4150] VGAM1813 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1813 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1813 host target RNA into VGAM1813 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4151] VGAM1814 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1814 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1814 host target RNA into VGAM1814 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4152] VGAM1815 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1815 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1815 host target RNA into VGAM1815 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4153] It is appreciated that a function of VGR3128 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3128 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3128 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3128 gene: VGAM1810 host target protein, VGAM1811 host target protein, VGAM1812 host target protein, VGAM1813 host target protein, VGAM1814 host target protein and VGAM1815 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1810, VGAM1811, VGAM1812, VGAM1813, VGAM1814 and VGAM1815. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3129(VGR3129) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4154] VGR3129 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3129 gene was detected is described hereinabove with reference to Figs. 1-9.

[4155] VGR3129 gene encodes VGR3129 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4156] VGR3129 precursor RNA folds spatially, forming VGR3129 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3129 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3129 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4157] VGR3129 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1816 precursor RNA, VGAM1817 precursor RNA, VGAM1818 precursor RNA, VGAM1819 precursor RNA, VGAM1820 precursor RNA, VGAM1821 precursor RNA, VGAM1822 precursor RNA and VGAM1823 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM

FOLDED PRECURSOR RNA of Fig. 1.

[4158] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1816 RNA, VGAM1817 RNA, VGAM1818 RNA, VGAM1819 RNA, VGAM1820 RNA, VGAM1821 RNA, VGAM1822 RNA and VGAM1823 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4159] VGAM1816 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1816 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1816 host target RNA into VGAM1816 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4160] VGAM1817 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1817 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1817 host target RNA into VGAM1817 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4161] VGAM1818 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1818 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1818 host target RNA into VGAM1818 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4162] VGAM1819 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1819 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1819 host target RNA into VGAM1819 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4163] VGAM1820 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1820 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1820 host target RNA into VGAM1820 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4164] VGAM1821 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1821 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1821 host target RNA into VGAM1821 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4165] VGAM1822 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1822 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1822 host target RNA into VGAM1822 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4166] VGAM1823 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1823 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1823 host target RNA into VGAM1823 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4167] It is appreciated that a function of VGR3129 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3129 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3129 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3129 gene: VGAM1816 host

target protein, VGAM1817 host target protein, VGAM1818 host target protein, VGAM1819 host target protein, VGAM1820 host target protein, VGAM1821 host target protein, VGAM1822 host target protein and VGAM1823 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1816, VGAM1817, VGAM1818, VGAM1819, VGAM1820, VGAM1821, VGAM1822 and VGAM1823. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3130 (VGR3130) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4168] VGR3130 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3130 gene was detected is described hereinabove with reference to Figs. 1-9.

[4169] VGR3130 gene encodes VGR3130 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4170] VGR3130 precursor RNA folds spatially, forming VGR3130 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3130 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3130 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4171] VGR3130 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1824 precursor RNA, VGAM1825 precursor RNA and VGAM1826 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4172] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1824 RNA, VGAM1825 RNA and VGAM1826 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4173] VGAM1824 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1824 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1824 host target RNA into VGAM1824 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4174] VGAM1825 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1825 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1825 host target RNA into VGAM1825 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4175] VGAM1826 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1826 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1826 host target RNA into VGAM1826 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4176] It is appreciated that a function of VGR3130 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3130 gene include

diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus. Specific functions, and accordingly utilities, of VGR3130 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3130 gene: VGAM1824 host target protein, VGAM1825 host target protein and VGAM1826 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1824, VGAM1825 and VGAM1826. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3131(VGR3131) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4177] VGR3131 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3131 gene was

detected is described hereinabove with reference to Figs. 1-9.

[4178] VGR3131 gene encodes VGR3131 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4179] VGR3131 precursor RNA folds spatially, forming VGR3131 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3131 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3131 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4180] VGR3131 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1827 precursor RNA, VGAM1828 precursor RNA and VGAM1829 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4181] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1827 RNA, VGAM1828 RNA and VGAM1829 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4182] VGAM1827 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1827 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1827 host target RNA into VGAM1827 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4183] VGAM1828 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1828 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1828 host target RNA into VGAM1828 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4184] VGAM1829 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1829 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1829 host target RNA into VGAM1829 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4185] It is appreciated that a function of VGR3131 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3131 gene include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGR3131 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3131 gene: VGAM1827 host target protein, VGAM1828 host target protein and VGAM1829 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1827, VGAM1828 and VGAM1829. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3132(VGR3132) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4186] VGR3132 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3132 gene was detected is described hereinabove with reference to Figs. 1–9.

[4187] VGR3132 gene encodes VGR3132 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4188] VGR3132 precursor RNA folds spatially, forming VGR3132 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3132 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3132 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4189] VGR3132 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1830 precursor RNA, VGAM1831 precursor RNA, VGAM1832 precursor RNA, VGAM1833

precursor RNA and VGAM1834 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4190] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1830 RNA, VGAM1831 RNA, VGAM1832 RNA, VGAM1833 RNA and VGAM1834 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4191] VGAM1830 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1830 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1830 host target RNA into VGAM1830 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4192] VGAM1831 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1831 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1831 host target RNA into VGAM1831 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4193] VGAM1832 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1832 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1832 host target RNA into

VGAM1832 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4194] VGAM1833 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1833 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1833 host target RNA into VGAM1833 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4195] VGAM1834 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1834 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1834 host target RNA into VGAM1834 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4196] It is appreciated that a function of VGR3132 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3132 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3132 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3132 gene: VGAM1830 host target protein, VGAM1831 host target protein, VGAM1832 host target protein, VGAM1833 host target protein and VGAM1834 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1830, VGAM1831, VGAM1832, VGAM1833 and VGAM1834. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory vi-

ral gene, referred to here as Viral Genomic Record 3133(VGR3133) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4197] VGR3133 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3133 gene was detected is described hereinabove with reference to Figs. 1-9.

[4198] VGR3133 gene encodes VGR3133 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4199] VGR3133 precursor RNA folds spatially, forming VGR3133 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3133 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3133 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4200] VGR3133 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1835 precursor RNA, VGAM1836 precursor RNA, VGAM1837 precursor RNA, VGAM1838 precursor RNA and VGAM1839 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4201] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1835 RNA, VGAM1836 RNA, VGAM1837 RNA, VGAM1838 RNA and VGAM1839 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4202] VGAM1835 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1835 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1835 host target RNA into VGAM1835 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4203] VGAM1836 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1836 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1836 host target RNA into VGAM1836 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4204] VGAM1837 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1837 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1837 host target RNA into VGAM1837 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4205] VGAM1838 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1838 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1838 host target RNA into VGAM1838 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4206] VGAM1839 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1839 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1839 host target RNA into VGAM1839 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4207] It is appreciated that a function of VGR3133 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3133 gene include diagnosis, prevention and treatment of viral infection by Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3133 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3133 gene: VGAM1835 host target protein, VGAM1836 host target protein, VGAM1837 host target protein, VGAM1838 host target protein and VGAM1839 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1835, VGAM1836, VGAM1837, VGAM1838 and VGAM1839. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3134(VGR3134) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4208] VGR3134 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3134 gene was detected is described hereinabove with reference to Figs. 1-9.

[4209] VGR3134 gene encodes VGR3134 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4210] VGR3134 precursor RNA folds spatially, forming VGR3134 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3134 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3134 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4211] VGR3134 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1840 precursor RNA and VGAM1841 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4212] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1840 RNA and VGAM1841 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4213] VGAM1840 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1840 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1840 host target RNA into VGAM1840 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4214] VGAM1841 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1841 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1841 host target RNA into VGAM1841 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4215] It is appreciated that a function of VGR3134 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3134 gene include diagnosis, prevention and treatment of viral infection by Cowpea Mottle Virus. Specific functions, and accordingly utilities, of VGR3134 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3134 gene: VGAM1840 host target protein and VGAM1841 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1840 and VGAM1841. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3135(VGR3135) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4216] VGR3135 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3135 gene was detected is described hereinabove with reference to Figs. 1–9.

[4217] VGR3135 gene encodes VGR3135 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4218] VGR3135 precursor RNA folds spatially, forming VGR3135 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3135 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3135 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4219] VGR3135 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM1842 precursor RNA, VGAM1843 precursor RNA, VGAM1844 precursor RNA, VGAM1845

precursor RNA and VGAM1846 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4220] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1842 RNA, VGAM1843 RNA, VGAM1844 RNA, VGAM1845 RNA and VGAM1846 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4221] VGAM1842 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1842 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1842 host target RNA into VGAM1842 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4222] VGAM1843 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1843 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1843 host target RNA into VGAM1843 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4223] VGAM1844 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1844 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1844 host target RNA into

VGAM1844 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4224] VGAM1845 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1845 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1845 host target RNA into VGAM1845 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4225] VGAM1846 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1846 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1846 host target RNA into VGAM1846 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4226] It is appreciated that a function of VGR3135 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3135 gene include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3135 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3135 gene: VGAM1842 host target protein, VGAM1843 host target protein, VGAM1844 host target protein, VGAM1845 host target protein and VGAM1846 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1842, VGAM1843, VGAM1844, VGAM1845 and VGAM1846. Fig. 9 further provides a conceptual description of novel bioinformatically detected

regulatory viral gene, referred to here as Viral Genomic Record 3136(VGR3136) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4227] VGR3136 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3136 gene was detected is described hereinabove with reference to Figs. 1-9.

[4228] VGR3136 gene encodes VGR3136 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4229] VGR3136 precursor RNA folds spatially, forming VGR3136 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3136 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3136 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4230] VGR3136 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1847 precursor RNA, VGAM1848 precursor RNA, VGAM1849 precursor RNA, VGAM1850 precursor RNA, VGAM1851 precursor RNA, VGAM1852 precursor RNA and VGAM1853 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4231] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1847 RNA, VGAM1848 RNA, VGAM1849 RNA, VGAM1850 RNA, VGAM1851 RNA, VGAM1852 RNA and VGAM1853 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4232] VGAM1847 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1847 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1847 host target RNA into VGAM1847 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4233] VGAM1848 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1848 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1848 host target RNA into VGAM1848 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4234] VGAM1849 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1849 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1849 host target RNA into VGAM1849 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4235] VGAM1850 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1850 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1850 host target RNA into VGAM1850 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4236] VGAM1851 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1851 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1851 host target RNA into VGAM1851 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4237] VGAM1852 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1852 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1852 host target RNA into VGAM1852 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4238] VGAM1853 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1853 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1853 host target RNA into VGAM1853 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4239] It is appreciated that a function of VGR3136 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3136 gene include diagnosis, prevention and treatment of viral infection by Sonchus Yellow Net Virus. Specific functions, and accordingly utilities, of VGR3136 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3136 gene: VGAM1847 host

target protein, VGAM1848 host target protein, VGAM1849 host target protein, VGAM1850 host target protein, VGAM1851 host target protein, VGAM1852 host target protein and VGAM1853 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1847, VGAM1848, VGAM1849, VGAM1850, VGAM1851, VGAM1852 and VGAM1853. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3137(VGR3137) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4240] VGR3137 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3137 gene was detected is described hereinabove with reference to Figs. 1-9.

[4241] VGR3137 gene encodes VGR3137 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4242] VGR3137 precursor RNA folds spatially, forming VGR3137 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3137 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3137 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4243] VGR3137 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1854 precursor RNA and VGAM1855 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4244] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM1854 RNA and VGAM1855 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4245] VGAM1854 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1854 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1854 host target RNA into VGAM1854 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4246] VGAM1855 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1855 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1855 host target RNA into VGAM1855 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4247] It is appreciated that a function of VGR3137 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3137 gene include diagnosis, prevention and treatment of viral infection by Cowpea Chlorotic Mottle Virus. Specific functions, and accordingly utilities, of VGR3137 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3137 gene: VGAM1854 host target protein and VGAM1855 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1854 and VGAM1855. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3138(VGR3138) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4248] VGR3138 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3138 gene was detected is described hereinabove with reference to Figs. 1-9.

[4249] VGR3138 gene encodes VGR3138 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4250] VGR3138 precursor RNA folds spatially, forming VGR3138 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3138 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3138 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[4251] VGR3138 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1856 precursor RNA, VGAM1857 precursor RNA, VGAM1858 precursor RNA, VGAM1859 precursor RNA, VGAM1860 precursor RNA and VGAM1861 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4252] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1856 RNA, VGAM1857 RNA, VGAM1858 RNA, VGAM1859 RNA, VGAM1860 RNA and VGAM1861 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4253] VGAM1856 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1856 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1856 host target RNA into VGAM1856 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4254] VGAM1857 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1857 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1857 host target RNA into VGAM1857 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4255] VGAM1858 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1858 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1858 host target RNA into VGAM1858 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4256] VGAM1859 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1859 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1859 host target RNA into VGAM1859 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4257] VGAM1860 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1860 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1860 host target RNA into VGAM1860 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4258] VGAM1861 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1861 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1861 host target RNA into VGAM1861 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4259] It is appreciated that a function of VGR3138 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3138 gene include diagnosis, prevention and treatment of viral infection by Rice Yellow Stunt Virus. Specific functions, and accordingly utilities, of VGR3138 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3138 gene: VGAM1856 host target protein, VGAM1857 host target protein, VGAM1858 host target protein, VGAM1859 host target protein, VGAM1860 host target protein and VGAM1861 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1856, VGAM1857, VGAM1858, VGAM1859, VGAM1860 and VGAM1861. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3139(VGR3139) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function

and utility of which at least one host target gene is known in the art.

[4260] VGR3139 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3139 gene was detected is described hereinabove with reference to Figs. 1-9.

[4261] VGR3139 gene encodes VGR3139 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4262] VGR3139 precursor RNA folds spatially, forming VGR3139 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3139 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3139 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4263] VGR3139 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM

precursor RNAs, VGAM1863 precursor RNA, VGAM1864 precursor RNA, VGAM1865 precursor RNA, VGAM1866 precursor RNA, VGAM1867 precursor RNA and VGAM1868 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4264] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1863 RNA, VGAM1864 RNA, VGAM1865 RNA, VGAM1866 RNA, VGAM1867 RNA and VGAM1868 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4265] VGAM1863 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1863 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1863 host target RNA into VGAM1863 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4266] VGAM1864 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1864 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1864 host target RNA into VGAM1864 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4267] VGAM1865 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1865 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1865 host target RNA into VGAM1865 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4268] VGAM1866 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1866 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1866 host target RNA into VGAM1866 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4269] VGAM1867 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1867 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1867 host target RNA into VGAM1867 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4270] VGAM1868 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1868 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1868 host target RNA into VGAM1868 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4271] It is appreciated that a function of VGR3139 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3139 gene include

diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3139 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3139 gene: VGAM1863 host target protein, VGAM1864 host target protein, VGAM1865 host target protein, VGAM1866 host target protein, VGAM1867 host target protein and VGAM1868 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1863, VGAM1864, VGAM1865, VGAM1866, VGAM1867 and VGAM1868. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3140(VGR3140) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4272] VGR3140 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3140 gene was detected is described hereinabove with reference to Figs. 1-9.

[4273] VGR3140 gene encodes VGR3140 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4274] VGR3140 precursor RNA folds spatially, forming VGR3140 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3140 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3140 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4275] VGR3140 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1870 precursor RNA, VGAM1871 precursor RNA, VGAM1872 precursor RNA, VGAM1873 precursor RNA, VGAM1874 precursor RNA, VGAM1875

precursor RNA, VGAM1876 precursor RNA and VGAM1877 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4276] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1870 RNA, VGAM1871 RNA, VGAM1872 RNA, VGAM1873 RNA, VGAM1874 RNA, VGAM1875 RNA, VGAM1876 RNA and VGAM1877 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4277] VGAM1870 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1870 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1870 host target RNA into

VGAM1870 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4278] VGAM1871 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1871 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1871 host target RNA into VGAM1871 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4279] VGAM1872 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1872 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1872 host target RNA into VGAM1872 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4280] VGAM1873 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1873 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1873 host target RNA into VGAM1873 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4281] VGAM1874 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1874 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1874 host target RNA into VGAM1874 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4282] VGAM1875 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1875 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1875 host target RNA into VGAM1875 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4283] VGAM1876 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1876 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1876 host target RNA into VGAM1876 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4284] VGAM1877 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1877 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1877 host target RNA into VGAM1877 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4285] It is appreciated that a function of VGR3140 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3140 gene include diagnosis, prevention and treatment of viral infection by

Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3140 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3140 gene: VGAM1870 host target protein, VGAM1871 host target protein, VGAM1872 host target protein, VGAM1873 host target protein, VGAM1874 host target protein, VGAM1875 host target protein, VGAM1876 host target protein and VGAM1877 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1870, VGAM1871, VGAM1872, VGAM1873, VGAM1874, VGAM1875, VGAM1876 and VGAM1877. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3141(VGR3141) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4286] VGR3141 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3141 gene was detected is described hereinabove with reference to Figs. 1-9.

[4287] VGR3141 gene encodes VGR3141 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4288] VGR3141 precursor RNA folds spatially, forming VGR3141 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3141 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3141 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4289] VGR3141 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1878 precursor RNA, VGAM1879 precursor RNA, VGAM1880 precursor RNA, VGAM1881 precursor RNA, VGAM1882 precursor RNA, VGAM1883

precursor RNA and VGAM1884 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4290] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1878 RNA, VGAM1879 RNA, VGAM1880 RNA, VGAM1881 RNA, VGAM1882 RNA, VGAM1883 RNA and VGAM1884 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4291] VGAM1878 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1878 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1878 host target RNA into

VGAM1878 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4292] VGAM1879 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1879 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1879 host target RNA into VGAM1879 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4293] VGAM1880 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1880 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1880 host target RNA into VGAM1880 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4294] VGAM1881 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1881 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1881 host target RNA into VGAM1881 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4295] VGAM1882 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1882 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1882 host target RNA into VGAM1882 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4296] VGAM1883 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1883 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1883 host target RNA into VGAM1883 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4297] VGAM1884 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1884 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1884 host target RNA into VGAM1884 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4298] It is appreciated that a function of VGR3141 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3141 gene include diagnosis, prevention and treatment of viral infection by Bovine Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGR3141 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3141 gene: VGAM1878 host target protein, VGAM1879 host target protein, VGAM1880 host target protein, VGAM1881 host target protein, VGAM1882 host target protein, VGAM1883 host target protein and VGAM1884 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove

with reference to VGAM1878, VGAM1879, VGAM1880, VGAM1881, VGAM1882, VGAM1883 and VGAM1884. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3142(VGR3142) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4299] VGR3142 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3142 gene was detected is described hereinabove with reference to Figs. 1-9.

[4300] VGR3142 gene encodes VGR3142 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4301] VGR3142 precursor RNA folds spatially, forming VGR3142 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3142 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3142 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4302] VGR3142 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1885 precursor RNA, VGAM1886 precursor RNA, VGAM1887 precursor RNA, VGAM1888 precursor RNA, VGAM1889 precursor RNA, VGAM1890 precursor RNA and VGAM1891 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4303] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1885 RNA, VGAM1886 RNA, VGAM1887 RNA, VGAM1888 RNA, VGAM1889 RNA, VGAM1890 RNA and VGAM1891 RNA, herein schematically represented by VGAM1 RNA through

VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4304] VGAM1885 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1885 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1885 host target RNA into VGAM1885 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4305] VGAM1886 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1886 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1886 host target RNA into

VGAM1886 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4306] VGAM1887 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1887 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1887 host target RNA into VGAM1887 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4307] VGAM1888 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1888 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1888 host target RNA into VGAM1888 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4308] VGAM1889 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1889 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1889 host target RNA into VGAM1889 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4309] VGAM1890 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1890 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1890 host target RNA into VGAM1890 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4310] VGAM1891 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1891 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1891 host target RNA into VGAM1891 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4311] It is appreciated that a function of VGR3142 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3142 gene include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accord-

ingly utilities, of VGR3142 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3142 gene: VGAM1885 host target protein, VGAM1886 host target protein, VGAM1887 host target protein, VGAM1888 host target protein, VGAM1889 host target protein, VGAM1890 host target protein and VGAM1891 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1885, VGAM1886, VGAM1887, VGAM1888, VGAM1889, VGAM1890 and VGAM1891. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3143(VGR3143) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4312] VGR3143 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding,

RNA viral gene. The method by which VGR3143 gene was detected is described hereinabove with reference to Figs. 1–9.

[4313] VGR3143 gene encodes VGR3143 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4314] VGR3143 precursor RNA folds spatially, forming VGR3143 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3143 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3143 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4315] VGR3143 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1892 precursor RNA and VGAM1893 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs

being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4316] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1892 RNA and VGAM1893 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4317] VGAM1892 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1892 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1892 host target RNA into VGAM1892 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4318] VGAM1893 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1893 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1893 host target RNA into VGAM1893 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4319] It is appreciated that a function of VGR3143 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3143 gene include diagnosis, prevention and treatment of viral infection by Newcastle Disease Virus. Specific functions, and accordingly utilities, of VGR3143 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3143 gene: VGAM1892 host target protein and VGAM1893 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove

with reference to VGAM1892 and VGAM1893. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3144(VGR3144) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4320] VGR3144 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3144 gene was detected is described hereinabove with reference to Figs. 1-9.

[4321] VGR3144 gene encodes VGR3144 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4322] VGR3144 precursor RNA folds spatially, forming VGR3144 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3144 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3144 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4323] VGR3144 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1894 precursor RNA, VGAM1895 precursor RNA, VGAM1896 precursor RNA, VGAM1897 precursor RNA, VGAM1898 precursor RNA, VGAM1899 precursor RNA, VGAM1900 precursor RNA and VGAM1901 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4324] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1894 RNA, VGAM1895 RNA, VGAM1896 RNA, VGAM1897 RNA, VGAM1898 RNA, VGAM1899 RNA, VGAM1900 RNA and VGAM1901 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM

RNAs corresponding to VGAM RNA of Fig. 1.

[4325] VGAM1894 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1894 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1894 host target RNA into VGAM1894 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4326] VGAM1895 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1895 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1895 host target RNA into VGAM1895 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4327] VGAM1896 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1896 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1896 host target RNA into VGAM1896 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4328] VGAM1897 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1897 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1897 host target RNA into

VGAM1897 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4329] VGAM1898 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1898 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1898 host target RNA into VGAM1898 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4330] VGAM1899 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1899 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1899 host target RNA into VGAM1899 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4331] VGAM1900 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1900 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1900 host target RNA into VGAM1900 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4332] VGAM1901 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1901 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1901 host target RNA into VGAM1901 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4333] It is appreciated that a function of VGR3144 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3144 gene include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGR3144 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3144 gene: VGAM1894 host target protein, VGAM1895 host target protein, VGAM1896 host target protein, VGAM1897 host target protein, VGAM1898 host target protein, VGAM1899 host target protein, VGAM1900 host target protein and VGAM1901 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with refer-

ence to VGAM1894, VGAM1895, VGAM1896, VGAM1897, VGAM1898, VGAM1899, VGAM1900 and VGAM1901. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3145(VGR3145) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4334] VGR3145 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3145 gene was detected is described hereinabove with reference to Figs. 1-9.

[4335] VGR3145 gene encodes VGR3145 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4336] VGR3145 precursor RNA folds spatially, forming VGR3145 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3145 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3145 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4337] VGR3145 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1902 precursor RNA, VGAM1903 precursor RNA and VGAM1904 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4338] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1902 RNA, VGAM1903 RNA and VGAM1904 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4339] VGAM1902 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1902 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1902 host target RNA into VGAM1902 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4340] VGAM1903 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1903 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1903 host target RNA into VGAM1903 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4341] VGAM1904 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1904 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1904 host target RNA into VGAM1904 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4342] It is appreciated that a function of VGR3145 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3145 gene include diagnosis, prevention and treatment of viral infection by Respiratory Syncytial Virus. Specific functions, and accordingly utilities, of VGR3145 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3145 gene: VGAM1902 host target protein, VGAM1903 host target protein and

VGAM1904 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1902, VGAM1903 and VGAM1904. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3146(VGR3146) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4343] VGR3146 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3146 gene was detected is described hereinabove with reference to Figs. 1-9.

[4344] VGR3146 gene encodes VGR3146 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4345] VGR3146 precursor RNA folds spatially, forming VGR3146 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3146 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3146 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4346] VGR3146 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1905 precursor RNA and VGAM1906 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4347] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1905 RNA and VGAM1906 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4348] VGAM1905 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1905 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1905 host target RNA into VGAM1905 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4349] VGAM1906 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1906 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1906 host target RNA into VGAM1906 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4350] It is appreciated that a function of VGR3146 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3146 gene include diagnosis, prevention and treatment of viral infection by Sendai Virus. Specific functions, and accordingly utilities, of VGR3146 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3146 gene: VGAM1905 host target protein and VGAM1906 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1905 and VGAM1906. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3147(VGR3147) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4351] VGR3147 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3147 gene was detected is described hereinabove with reference to Figs. 1-9.

[4352] VGR3147 gene encodes VGR3147 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4353] VGR3147 precursor RNA folds spatially, forming VGR3147 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3147 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3147 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4354] VGR3147 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1907 precursor RNA, VGAM1908 precursor RNA, VGAM1909 precursor RNA, VGAM1910

precursor RNA, VGAM1911 precursor RNA, VGAM1912 precursor RNA and VGAM1913 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4355] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1907 RNA, VGAM1908 RNA, VGAM1909 RNA, VGAM1910 RNA, VGAM1911 RNA, VGAM1912 RNA and VGAM1913 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4356] VGAM1907 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1907 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1907 host target RNA into VGAM1907 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4357] VGAM1908 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1908 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1908 host target RNA into VGAM1908 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4358] VGAM1909 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1909 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1909 host target RNA into VGAM1909 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4359] VGAM1910 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1910 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1910 host target RNA into VGAM1910 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4360] VGAM1911 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1911 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1911 host target RNA into VGAM1911 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4361] VGAM1912 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1912 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1912 host target RNA into VGAM1912 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4362] VGAM1913 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1913 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1913 host target RNA into VGAM1913 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4363] It is appreciated that a function of VGR3147 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3147 gene include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGR3147 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3147 gene: VGAM1907 host target protein, VGAM1908 host target protein, VGAM1909 host target protein, VGAM1910 host target protein, VGAM1911 host target protein, VGAM1912 host target protein and VGAM1913 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM1907, VGAM1908, VGAM1909, VGAM1910, VGAM1911, VGAM1912 and VGAM1913. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3148(VGR3148) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4364] VGR3148 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3148 gene was detected is described hereinabove with reference to Figs. 1-9.

[4365] VGR3148 gene encodes VGR3148 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4366] VGR3148 precursor RNA folds spatially, forming VGR3148 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3148 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3148 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4367] VGR3148 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1914 precursor RNA and VGAM1915 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4368] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1914 RNA and VGAM1915 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4369] VGAM1914 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1914 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1914 host target RNA into VGAM1914 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4370] VGAM1915 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1915 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1915 host target RNA into VGAM1915 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4371] It is appreciated that a function of VGR3148 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3148 gene include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 3. Specific functions, and accordingly utilities, of VGR3148 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3148 gene: VGAM1914 host target protein and VGAM1915 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1914 and VGAM1915. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3149(VGR3149) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4372] VGR3149 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3149 gene was detected is described hereinabove with reference to Figs. 1-9.

[4373] VGR3149 gene encodes VGR3149 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4374] VGR3149 precursor RNA folds spatially, forming VGR3149 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3149 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3149 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4375] VGR3149 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1916 precursor RNA, VGAM1917 precursor RNA and VGAM1918 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4376] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1916 RNA, VGAM1917 RNA and VGAM1918 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4377] VGAM1916 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1916 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1916 host target RNA into VGAM1916 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4378] VGAM1917 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1917 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1917 host target RNA into VGAM1917 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4379] VGAM1918 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1918 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1918 host target RNA into VGAM1918 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4380] It is appreciated that a function of VGR3149 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3149 gene include diagnosis, prevention and treatment of viral infection by Human Parainfluenza Virus 1 Strain Washington/1964. Specific functions, and accordingly utilities, of VGR3149 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3149 gene: VGAM1916 host target protein, VGAM1917 host target protein and VGAM1918 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1916, VGAM1917 and VGAM1918. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3150(VGR3150) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[4381] VGR3150 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3150 gene was detected is described hereinabove with reference to Figs. 1-9.

[4382] VGR3150 gene encodes VGR3150 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4383] VGR3150 precursor RNA folds spatially, forming VGR3150 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3150 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3150 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4384] VGR3150 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM

precursor RNAs, VGAM1920 precursor RNA, VGAM1921 precursor RNA, VGAM1922 precursor RNA, VGAM1923 precursor RNA, VGAM1924 precursor RNA, VGAM1925 precursor RNA and VGAM1926 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4385] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1920 RNA, VGAM1921 RNA, VGAM1922 RNA, VGAM1923 RNA, VGAM1924 RNA, VGAM1925 RNA and VGAM1926 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4386] VGAM1920 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1920 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1920 host target RNA into VGAM1920 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4387] VGAM1921 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1921 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1921 host target RNA into VGAM1921 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4388] VGAM1922 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1922 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1922 host target RNA into VGAM1922 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4389] VGAM1923 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1923 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1923 host target RNA into VGAM1923 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4390] VGAM1924 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1924 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1924 host target RNA into VGAM1924 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4391] VGAM1925 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1925 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1925 host target RNA into VGAM1925 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4392] VGAM1926 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1926 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1926 host target RNA into VGAM1926 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4393] It is appreciated that a function of VGR3150 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3150 gene include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGR3150 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3150 gene: VGAM1920 host target protein, VGAM1921 host target protein, VGAM1922 host target protein, VGAM1923 host target protein, VGAM1924 host target protein, VGAM1925 host target protein and VGAM1926 host target protein, herein

schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1920, VGAM1921, VGAM1922, VGAM1923, VGAM1924, VGAM1925 and VGAM1926. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3151(VGR3151) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4394] VGR3151 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3151 gene was detected is described hereinabove with reference to Figs. 1-9.

[4395] VGR3151 gene encodes VGR3151 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4396] VGR3151 precursor RNA folds spatially, forming VGR3151 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3151 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3151 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4397] VGR3151 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1927 precursor RNA and VGAM1928 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4398] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1927 RNA and VGAM1928 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4399] VGAM1927 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1927 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1927 host target RNA into VGAM1927 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4400] VGAM1928 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1928 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1928 host target RNA into VGAM1928 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4401] It is appreciated that a function of VGR3151 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3151 gene include diagnosis, prevention and treatment of viral infection by Canine Distemper Virus. Specific functions, and accordingly utilities, of VGR3151 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3151 gene: VGAM1927 host target protein and VGAM1928 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1927 and VGAM1928. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3152(VGR3152) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in

the art.

[4402] VGR3152 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3152 gene was detected is described hereinabove with reference to Figs. 1-9.

[4403] VGR3152 gene encodes VGR3152 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4404] VGR3152 precursor RNA folds spatially, forming VGR3152 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3152 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3152 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4405] VGR3152 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1930 precursor RNA, VGAM1931

precursor RNA, VGAM1932 precursor RNA, VGAM1933 precursor RNA, VGAM1934 precursor RNA, VGAM1935 precursor RNA and VGAM1936 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4406] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1930 RNA, VGAM1931 RNA, VGAM1932 RNA, VGAM1933 RNA, VGAM1934 RNA, VGAM1935 RNA and VGAM1936 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4407] VGAM1930 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1930 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1930 host target RNA into VGAM1930 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4408] VGAM1931 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1931 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1931 host target RNA into VGAM1931 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4409] VGAM1932 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1932 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1932 host target RNA into VGAM1932 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4410] VGAM1933 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1933 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1933 host target RNA into VGAM1933 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4411] VGAM1934 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1934 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1934 host target RNA into VGAM1934 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4412] VGAM1935 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1935 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1935 host target RNA into VGAM1935 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4413] VGAM1936 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1936 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1936 host target RNA into VGAM1936 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4414] It is appreciated that a function of VGR3152 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3152 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3152 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3152 gene: VGAM1930 host target protein, VGAM1931 host target protein, VGAM1932 host target protein, VGAM1933 host target protein, VGAM1934 host target protein, VGAM1935 host target protein and VGAM1936 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1930, VGAM1931, VGAM1932, VGAM1933, VGAM1934, VGAM1935 and VGAM1936. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3153(VGR3153) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4415] VGR3153 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3153 gene was detected is described hereinabove with reference to Figs. 1-9.

[4416] VGR3153 gene encodes VGR3153 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4417] VGR3153 precursor RNA folds spatially, forming VGR3153 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3153 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3153 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4418] VGR3153 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1937 precursor RNA and VGAM1938 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4419] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1937 RNA and VGAM1938 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4420] VGAM1937 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1937 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1937 host target RNA into VGAM1937 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4421] VGAM1938 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1938 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1938 host target RNA into VGAM1938 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4422] It is appreciated that a function of VGR3153 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3153 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3153 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3153 gene: VGAM1937 host target protein and VGAM1938 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1937 and VGAM1938. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3154(VGR3154) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4423] VGR3154 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3154 gene was detected is described hereinabove with reference to Figs. 1-9.

[4424] VGR3154 gene encodes VGR3154 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4425] VGR3154 precursor RNA folds spatially, forming VGR3154 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3154 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3154 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4426] VGR3154 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1940 precursor RNA, VGAM1941 precursor RNA, VGAM1942 precursor RNA, VGAM1943

precursor RNA, VGAM1944 precursor RNA, VGAM1945 precursor RNA, VGAM1946 precursor RNA and VGAM1947 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4427] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1940 RNA, VGAM1941 RNA, VGAM1942 RNA, VGAM1943 RNA, VGAM1944 RNA, VGAM1945 RNA, VGAM1946 RNA and VGAM1947 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4428] VGAM1940 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1940 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1940 host target RNA into VGAM1940 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4429] VGAM1941 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1941 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1941 host target RNA into VGAM1941 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4430] VGAM1942 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1942 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1942 host target RNA into VGAM1942 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4431] VGAM1943 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1943 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1943 host target RNA into VGAM1943 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4432] VGAM1944 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1944 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1944 host target RNA into VGAM1944 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4433] VGAM1945 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1945 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1945 host target RNA into VGAM1945 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4434] VGAM1946 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1946 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1946 host target RNA into VGAM1946 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4435] VGAM1947 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1947 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1947 host target RNA into VGAM1947 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4436] It is appreciated that a function of VGR3154 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3154 gene include

diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR3154 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3154 gene: VGAM1940 host target protein, VGAM1941 host target protein, VGAM1942 host target protein, VGAM1943 host target protein, VGAM1944 host target protein, VGAM1945 host target protein, VGAM1946 host target protein and VGAM1947 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM1940, VGAM1941, VGAM1942, VGAM1943, VGAM1944, VGAM1945, VGAM1946 and VGAM1947. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3155(VGR3155) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4437] VGR3155 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3155 gene was detected is described hereinabove with reference to Figs. 1–9.

[4438] VGR3155 gene encodes VGR3155 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4439] VGR3155 precursor RNA folds spatially, forming VGR3155 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3155 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3155 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4440] VGR3155 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1948 precursor RNA, VGAM1949 precursor RNA, VGAM1950 precursor RNA, VGAM1951

precursor RNA, VGAM1952 precursor RNA, VGAM1953 precursor RNA and VGAM1954 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4441] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1948 RNA, VGAM1949 RNA, VGAM1950 RNA, VGAM1951 RNA, VGAM1952 RNA, VGAM1953 RNA and VGAM1954 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4442] VGAM1948 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1948 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1948 host target RNA into VGAM1948 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4443] VGAM1949 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1949 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1949 host target RNA into VGAM1949 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4444] VGAM1950 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1950 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1950 host target RNA into VGAM1950 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4445] VGAM1951 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1951 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1951 host target RNA into VGAM1951 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4446] VGAM1952 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1952 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1952 host target RNA into VGAM1952 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4447] VGAM1953 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1953 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1953 host target RNA into VGAM1953 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4448] VGAM1954 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1954 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1954 host target RNA into VGAM1954 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4449] It is appreciated that a function of VGR3155 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3155 gene include diagnosis, prevention and treatment of viral infection by Avian Paramyxovirus 6. Specific functions, and accordingly utilities, of VGR3155 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3155 gene: VGAM1948 host target protein, VGAM1949 host target protein, VGAM1950 host target protein, VGAM1951 host target protein, VGAM1952 host target protein, VGAM1953 host target protein and VGAM1954 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM1948, VGAM1949, VGAM1950, VGAM1951, VGAM1952, VGAM1953 and VGAM1954. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3156(VGR3156) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4450] VGR3156 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3156 gene was detected is described hereinabove with reference to Figs. 1-9.

[4451] VGR3156 gene encodes VGR3156 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4452] VGR3156 precursor RNA folds spatially, forming VGR3156 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3156 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3156 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4453] VGR3156 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1955 precursor RNA, VGAM1956 precursor RNA, VGAM1957 precursor RNA, VGAM1958 precursor RNA, VGAM1959 precursor RNA and VGAM1960 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4454] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1955 RNA, VGAM1956 RNA, VGAM1957 RNA, VGAM1958 RNA, VGAM1959 RNA and VGAM1960 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA,

each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4455] VGAM1955 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1955 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1955 host target RNA into VGAM1955 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4456] VGAM1956 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1956 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1956 host target RNA into

VGAM1956 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4457] VGAM1957 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1957 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1957 host target RNA into VGAM1957 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4458] VGAM1958 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1958 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1958 host target RNA into VGAM1958 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4459] VGAM1959 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1959 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1959 host target RNA into VGAM1959 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4460] VGAM1960 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1960 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1960 host target RNA into VGAM1960 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4461] It is appreciated that a function of VGR3156 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3156 gene include diagnosis, prevention and treatment of viral infection by Macaca Mulatta Rhadinovirus. Specific functions, and accordingly utilities, of VGR3156 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3156 gene: VGAM1955 host target protein, VGAM1956 host target protein, VGAM1957 host target protein, VGAM1958 host target protein, VGAM1959 host target protein and VGAM1960 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1955, VGAM1956, VGAM1957, VGAM1958, VGAM1959 and

VGAM1960.Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3157(VGR3157) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4462] VGR3157 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3157 gene was detected is described hereinabove with reference to Figs. 1-9.

[4463] VGR3157 gene encodes VGR3157 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4464] VGR3157 precursor RNA folds spatially, forming VGR3157 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3157 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3157 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4465] VGR3157 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM1961 precursor RNA, VGAM1962 precursor RNA and VGAM1963 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4466] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1961 RNA, VGAM1962 RNA and VGAM1963 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4467] VGAM1961 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM1961 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1961 host target RNA into VGAM1961 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4468] VGAM1962 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1962 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1962 host target RNA into VGAM1962 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4469] VGAM1963 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1963 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1963 host target RNA into VGAM1963 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4470] It is appreciated that a function of VGR3157 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3157 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3157 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3157 gene: VGAM1961 host target protein, VGAM1962 host target protein and VGAM1963 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1961, VGAM1962 and VGAM1963. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3158(VGR3158) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4471] VGR3158 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3158 gene was detected is described hereinabove with reference to Figs. 1-9.

[4472] VGR3158 gene encodes VGR3158 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4473] VGR3158 precursor RNA folds spatially, forming VGR3158 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3158 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3158 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4474] VGR3158 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1964 precursor RNA, VGAM1965 precursor RNA, VGAM1966 precursor RNA, VGAM1967 precursor RNA, VGAM1968 precursor RNA, VGAM1969 precursor RNA, VGAM1970 precursor RNA and VGAM1971 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4475] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1964 RNA, VGAM1965 RNA, VGAM1966 RNA, VGAM1967 RNA, VGAM1968 RNA, VGAM1969 RNA, VGAM1970 RNA and

VGAM1971 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4476] VGAM1964 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1964 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1964 host target RNA into VGAM1964 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4477] VGAM1965 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1965 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1965 host target RNA into VGAM1965 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4478] VGAM1966 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1966 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1966 host target RNA into VGAM1966 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4479] VGAM1967 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1967 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1967 host target RNA into VGAM1967 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4480] VGAM1968 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1968 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1968 host target RNA into VGAM1968 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4481] VGAM1969 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1969 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1969 host target RNA into VGAM1969 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4482] VGAM1970 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1970 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1970 host target RNA into VGAM1970 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4483] VGAM1971 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1971 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1971 host target RNA into VGAM1971 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4484] It is appreciated that a function of VGR3158 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3158 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3158 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3158 gene: VGAM1964 host target protein, VGAM1965 host target protein, VGAM1966 host target protein, VGAM1967 host target protein, VGAM1968 host target protein, VGAM1969 host target protein, VGAM1970 host target protein and VGAM1971 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1964, VGAM1965, VGAM1966, VGAM1967, VGAM1968, VGAM1969, VGAM1970 and VGAM1971. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3159 (VGR3159) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4485] VGR3159 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3159 gene was detected is described hereinabove with reference to Figs. 1-9.

[4486] VGR3159 gene encodes VGR3159 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4487] VGR3159 precursor RNA folds spatially, forming VGR3159 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3159 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3159 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4488] VGR3159 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1972 precursor RNA, VGAM1973 precursor RNA, VGAM1974 precursor RNA, VGAM1975 precursor RNA, VGAM1976 precursor RNA, VGAM1977 precursor RNA and VGAM1978 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4489] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1972 RNA, VGAM1973 RNA, VGAM1974 RNA, VGAM1975 RNA, VGAM1976 RNA, VGAM1977 RNA and VGAM1978 RNA,

herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4490] VGAM1972 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1972 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1972 host target RNA into VGAM1972 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4491] VGAM1973 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1973 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1973 host target RNA into VGAM1973 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4492] VGAM1974 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1974 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1974 host target RNA into VGAM1974 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4493] VGAM1975 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1975 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1975 host target RNA into VGAM1975 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4494] VGAM1976 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1976 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1976 host target RNA into VGAM1976 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4495] VGAM1977 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1977 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1977 host target RNA into VGAM1977 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4496] VGAM1978 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1978 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1978 host target RNA into VGAM1978 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4497] It is appreciated that a function of VGR3159 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3159 gene include diagnosis, prevention and treatment of viral infection by

Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3159 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3159 gene: VGAM1972 host target protein, VGAM1973 host target protein, VGAM1974 host target protein, VGAM1975 host target protein, VGAM1976 host target protein, VGAM1977 host target protein and VGAM1978 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1972, VGAM1973, VGAM1974, VGAM1975, VGAM1976, VGAM1977 and VGAM1978. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3160(VGR3160) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4498] VGR3160 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3160 gene was detected is described hereinabove with reference to Figs. 1-9.

[4499] VGR3160 gene encodes VGR3160 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4500] VGR3160 precursor RNA folds spatially, forming VGR3160 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3160 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3160 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4501] VGR3160 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1979 precursor RNA and VGAM1980 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3

FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4502] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1979 RNA and VGAM1980 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4503] VGAM1979 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1979 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1979 host target RNA into VGAM1979 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4504] VGAM1980 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1980 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1980 host target RNA into VGAM1980 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4505] It is appreciated that a function of VGR3160 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3160 gene include diagnosis, prevention and treatment of viral infection by Bovine Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3160 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3160 gene: VGAM1979 host target protein and VGAM1980 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM1979 and VGAM1980. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3161 (VGR3161) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4506] VGR3161 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3161 gene was detected is described hereinabove with reference to Figs. 1-9.

[4507] VGR3161 gene encodes VGR3161 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4508] VGR3161 precursor RNA folds spatially, forming VGR3161 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3161 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures

are due to the fact that the nucleotide sequence of VGR3161 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4509] VGR3161 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM1981 precursor RNA, VGAM1982 precursor RNA, VGAM1983 precursor RNA, VGAM1984 precursor RNA, VGAM1985 precursor RNA, VGAM1986 precursor RNA and VGAM1987 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4510] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1981 RNA, VGAM1982 RNA, VGAM1983 RNA, VGAM1984 RNA, VGAM1985 RNA, VGAM1986 RNA and VGAM1987 RNA, herein schematically represented by VGAM1 RNA through

VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4511] VGAM1981 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1981 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1981 host target RNA into VGAM1981 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4512] VGAM1982 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1982 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1982 host target RNA into

VGAM1982 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4513] VGAM1983 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1983 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1983 host target RNA into VGAM1983 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4514] VGAM1984 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1984 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM1984 host target RNA into VGAM1984 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4515] VGAM1985 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1985 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1985 host target RNA into VGAM1985 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4516] VGAM1986 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1986 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1986 host target RNA into VGAM1986 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4517] VGAM1987 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1987 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1987 host target RNA into VGAM1987 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4518] It is appreciated that a function of VGR3161 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3161 gene include diagnosis, prevention and treatment of viral infection by Hendra Virus. Specific functions, and accordingly utilities,

of VGR3161 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3161 gene: VGAM1981 host target protein, VGAM1982 host target protein, VGAM1983 host target protein, VGAM1984 host target protein, VGAM1985 host target protein, VGAM1986 host target protein and VGAM1987 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1981, VGAM1982, VGAM1983, VGAM1984, VGAM1985, VGAM1986 and VGAM1987. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3162(VGR3162) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4519] VGR3162 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3162 gene was

detected is described hereinabove with reference to Figs. 1-9.

[4520] VGR3162 gene encodes VGR3162 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4521] VGR3162 precursor RNA folds spatially, forming VGR3162 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3162 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3162 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4522] VGR3162 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM1988 precursor RNA and VGAM1989 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to

VGAM FOLDED PRECURSOR RNA of Fig. 1.

- [4523] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1988 RNA and VGAM1989 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.
- [4524] VGAM1988 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1988 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1988 host target RNA into VGAM1988 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.
- [4525] VGAM1989 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1989 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1989 host target RNA into VGAM1989 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4526] It is appreciated that a function of VGR3162 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3162 gene include diagnosis, prevention and treatment of viral infection by Hendra Virus. Specific functions, and accordingly utilities, of VGR3162 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3162 gene: VGAM1988 host target protein and VGAM1989 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1988 and VGAM1989. Fig. 9 further provides

a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3163(VGR3163) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4527] VGR3163 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3163 gene was detected is described hereinabove with reference to Figs. 1-9.

[4528] VGR3163 gene encodes VGR3163 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4529] VGR3163 precursor RNA folds spatially, forming VGR3163 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3163 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3163 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4530] VGR3163 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM1990 precursor RNA, VGAM1991 precursor RNA, VGAM1992 precursor RNA, VGAM1993 precursor RNA, VGAM1994 precursor RNA, VGAM1995 precursor RNA, VGAM1996 precursor RNA and VGAM1997 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4531] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1990 RNA, VGAM1991 RNA, VGAM1992 RNA, VGAM1993 RNA, VGAM1994 RNA, VGAM1995 RNA, VGAM1996 RNA and VGAM1997 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4532] VGAM1990 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1990 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1990 host target RNA into VGAM1990 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4533] VGAM1991 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1991 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1991 host target RNA into VGAM1991 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4534] VGAM1992 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1992 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1992 host target RNA into VGAM1992 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4535] VGAM1993 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1993 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1993 host target RNA into VGAM1993 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4536] VGAM1994 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1994 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1994 host target RNA into VGAM1994 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4537] VGAM1995 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1995 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1995 host target RNA into VGAM1995 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4538] VGAM1996 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1996 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1996 host target RNA into VGAM1996 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4539] VGAM1997 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1997 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1997 host target RNA into

VGAM1997 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4540] It is appreciated that a function of VGR3163 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3163 gene include diagnosis, prevention and treatment of viral infection by Nipah Virus. Specific functions, and accordingly utilities, of VGR3163 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3163 gene: VGAM1990 host target protein, VGAM1991 host target protein, VGAM1992 host target protein, VGAM1993 host target protein, VGAM1994 host target protein, VGAM1995 host target protein, VGAM1996 host target protein and VGAM1997 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1990, VGAM1991, VGAM1992, VGAM1993, VGAM1994, VGAM1995, VGAM1996 and VGAM1997. Fig. 9 further provides a con-

ceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3164(VGR3164) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4541] VGR3164 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3164 gene was detected is described hereinabove with reference to Figs. 1-9.

[4542] VGR3164 gene encodes VGR3164 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4543] VGR3164 precursor RNA folds spatially, forming VGR3164 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3164 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3164 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4544] VGR3164 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM1998 precursor RNA, VGAM1999 precursor RNA, VGAM2000 precursor RNA, VGAM2001 precursor RNA, VGAM2002 precursor RNA and VGAM2003 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4545] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM1998 RNA, VGAM1999 RNA, VGAM2000 RNA, VGAM2001 RNA, VGAM2002 RNA and VGAM2003 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4546] VGAM1998 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM1998 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1998 host target RNA into VGAM1998 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4547] VGAM1999 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM1999 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM1999 host target RNA into VGAM1999 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4548] VGAM2000 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2000 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2000 host target RNA into VGAM2000 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4549] VGAM2001 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2001 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2001 host target RNA into VGAM2001 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4550] VGAM2002 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2002 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2002 host target RNA into VGAM2002 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4551] VGAM2003 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2003 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2003 host target RNA into VGAM2003 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4552] It is appreciated that a function of VGR3164 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3164 gene include diagnosis, prevention and treatment of viral infection by Nipah Virus. Specific functions, and accordingly utilities, of VGR3164 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3164 gene: VGAM1998 host target protein, VGAM1999 host target protein, VGAM2000 host target protein, VGAM2001 host target protein, VGAM2002 host target protein and VGAM2003 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM1998, VGAM1999, VGAM2000, VGAM2001, VGAM2002 and VGAM2003. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3165(VGR3165) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4553] VGR3165 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3165 gene was detected is described hereinabove with reference to Figs. 1-9.

[4554] VGR3165 gene encodes VGR3165 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4555] VGR3165 precursor RNA folds spatially, forming VGR3165 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3165 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3165 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4556] VGR3165 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2004 precursor RNA, VGAM2005 precursor RNA and VGAM2006 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4557] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2004 RNA, VGAM2005 RNA and VGAM2006 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4558] VGAM2004 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2004 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2004 host target RNA into VGAM2004 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4559] VGAM2005 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2005 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2005 host target RNA into VGAM2005 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4560] VGAM2006 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2006 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2006 host target RNA into VGAM2006 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4561] It is appreciated that a function of VGR3165 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3165 gene include diagnosis, prevention and treatment of viral infection by Chimpanzee Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3165 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3165 gene: VGAM2004 host target protein, VGAM2005 host target protein and VGAM2006 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2004, VGAM2005 and VGAM2006. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to

here as Viral Genomic Record 3166(VGR3166) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4562] VGR3166 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3166 gene was detected is described hereinabove with reference to Figs. 1-9.

[4563] VGR3166 gene encodes VGR3166 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4564] VGR3166 precursor RNA folds spatially, forming VGR3166 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3166 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3166 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4565] VGR3166 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2007 precursor RNA, VGAM2008 precursor RNA, VGAM2009 precursor RNA, VGAM2010 precursor RNA, VGAM2011 precursor RNA, VGAM2012 precursor RNA, VGAM2013 precursor RNA and VGAM2014 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4566] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2007 RNA, VGAM2008 RNA, VGAM2009 RNA, VGAM2010 RNA, VGAM2011 RNA, VGAM2012 RNA, VGAM2013 RNA and VGAM2014 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4567] VGAM2007 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2007 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2007 host target RNA into VGAM2007 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4568] VGAM2008 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2008 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2008 host target RNA into VGAM2008 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4569] VGAM2009 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2009 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2009 host target RNA into VGAM2009 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4570] VGAM2010 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2010 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2010 host target RNA into VGAM2010 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4571] VGAM2011 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2011 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2011 host target RNA into VGAM2011 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4572] VGAM2012 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2012 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2012 host target RNA into VGAM2012 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4573] VGAM2013 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2013 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2013 host target RNA into VGAM2013 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4574] VGAM2014 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2014 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2014 host target RNA into VGAM2014 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4575] It is appreciated that a function of VGR3166 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3166 gene include diagnosis, prevention and treatment of viral infection by Reston Ebola Virus (REBOV). Specific functions, and accordingly utilities, of VGR3166 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3166 gene: VGAM2007 host target protein, VGAM2008 host target protein, VGAM2009 host target protein, VGAM2010 host target protein, VGAM2011 host target protein, VGAM2012 host target protein, VGAM2013 host target protein and VGAM2014 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2007, VGAM2008, VGAM2009, VGAM2010, VGAM2011, VGAM2012, VGAM2013 and VGAM2014. Fig. 9 further provides a conceptual description of novel

bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3167(VGR3167) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4576] VGR3167 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3167 gene was detected is described hereinabove with reference to Figs. 1-9.

[4577] VGR3167 gene encodes VGR3167 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4578] VGR3167 precursor RNA folds spatially, forming VGR3167 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3167 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3167 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4579] VGR3167 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2015 precursor RNA, VGAM2016 precursor RNA, VGAM2017 precursor RNA, VGAM2018 precursor RNA, VGAM2019 precursor RNA, VGAM2020 precursor RNA, VGAM2021 precursor RNA and VGAM2022 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4580] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2015 RNA, VGAM2016 RNA, VGAM2017 RNA, VGAM2018 RNA, VGAM2019 RNA, VGAM2020 RNA, VGAM2021 RNA and VGAM2022 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4581] VGAM2015 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2015 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2015 host target RNA into VGAM2015 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4582] VGAM2016 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2016 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2016 host target RNA into VGAM2016 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4583] VGAM2017 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2017 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2017 host target RNA into VGAM2017 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4584] VGAM2018 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2018 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2018 host target RNA into VGAM2018 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4585] VGAM2019 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2019 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2019 host target RNA into VGAM2019 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4586] VGAM2020 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2020 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2020 host target RNA into VGAM2020 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4587] VGAM2021 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2021 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2021 host target RNA into VGAM2021 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4588] VGAM2022 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2022 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2022 host target RNA into

VGAM2022 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4589] It is appreciated that a function of VGR3167 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3167 gene include diagnosis, prevention and treatment of viral infection by Kyuri Green Mottle Mosaic Virus. Specific functions, and accordingly utilities, of VGR3167 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3167 gene: VGAM2015 host target protein, VGAM2016 host target protein, VGAM2017 host target protein, VGAM2018 host target protein, VGAM2019 host target protein, VGAM2020 host target protein, VGAM2021 host target protein and VGAM2022 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2015, VGAM2016, VGAM2017, VGAM2018, VGAM2019, VGAM2020, VGAM2021 and VGAM2022. Fig.

9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3168(VGR3168) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4590] VGR3168 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3168 gene was detected is described hereinabove with reference to Figs. 1-9.

[4591] VGR3168 gene encodes VGR3168 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4592] VGR3168 precursor RNA folds spatially, forming VGR3168 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3168 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3168 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4593] VGR3168 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2023 precursor RNA, VGAM2024 precursor RNA, VGAM2025 precursor RNA, VGAM2026 precursor RNA, VGAM2027 precursor RNA, VGAM2028 precursor RNA, VGAM2029 precursor RNA and VGAM2030 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4594] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2023 RNA, VGAM2024 RNA, VGAM2025 RNA, VGAM2026 RNA, VGAM2027 RNA, VGAM2028 RNA, VGAM2029 RNA and VGAM2030 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4595] VGAM2023 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2023 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2023 host target RNA into VGAM2023 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4596] VGAM2024 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2024 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2024 host target RNA into VGAM2024 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4597] VGAM2025 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2025 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2025 host target RNA into VGAM2025 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4598] VGAM2026 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2026 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2026 host target RNA into VGAM2026 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4599] VGAM2027 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2027 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2027 host target RNA into VGAM2027 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4600] VGAM2028 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2028 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2028 host target RNA into

VGAM2028 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4601] VGAM2029 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2029 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2029 host target RNA into VGAM2029 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4602] VGAM2030 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2030 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2030 host target RNA into VGAM2030 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4603] It is appreciated that a function of VGR3168 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3168 gene include diagnosis, prevention and treatment of viral infection by Zaire Ebola Virus (ZEBOV). Specific functions, and accordingly utilities, of VGR3168 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3168 gene: VGAM2023 host target protein, VGAM2024 host target protein, VGAM2025 host target protein, VGAM2026 host target protein, VGAM2027 host target protein, VGAM2028 host target protein, VGAM2029 host target protein and VGAM2030 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2023, VGAM2024, VGAM2025, VGAM2026, VGAM2027,

VGAM2028, VGAM2029 and VGAM2030. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3169 (VGR3169) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4604] VGR3169 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3169 gene was detected is described hereinabove with reference to Figs. 1-9.

[4605] VGR3169 gene encodes VGR3169 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4606] VGR3169 precursor RNA folds spatially, forming VGR3169 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3169 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3169 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4607] VGR3169 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2031 precursor RNA, VGAM2032 precursor RNA, VGAM2033 precursor RNA, VGAM2034 precursor RNA and VGAM2035 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4608] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2031 RNA, VGAM2032 RNA, VGAM2033 RNA, VGAM2034 RNA and VGAM2035 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4609] VGAM2031 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2031 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2031 host target RNA into VGAM2031 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4610] VGAM2032 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2032 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2032 host target RNA into VGAM2032 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4611] VGAM2033 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2033 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2033 host target RNA into VGAM2033 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4612] VGAM2034 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2034 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2034 host target RNA into VGAM2034 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4613] VGAM2035 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2035 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2035 host target RNA into VGAM2035 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4614] It is appreciated that a function of VGR3169 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3169 gene include diagnosis, prevention and treatment of viral infection by Zaire Ebola Virus (ZEBOV). Specific functions, and accordingly utilities, of VGR3169 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3169 gene: VGAM2031 host target protein, VGAM2032 host target protein, VGAM2033

host target protein, VGAM2034 host target protein and VGAM2035 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2031, VGAM2032, VGAM2033, VGAM2034 and VGAM2035. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3170(VGR3170) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4615] VGR3170 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3170 gene was detected is described hereinabove with reference to Figs. 1-9.

[4616] VGR3170 gene encodes VGR3170 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4617] VGR3170 precursor RNA folds spatially, forming VGR3170

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3170 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3170 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4618] VGR3170 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2036 precursor RNA, VGAM2037 precursor RNA, VGAM2038 precursor RNA, VGAM2039 precursor RNA, VGAM2040 precursor RNA and VGAM2041 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4619] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2036

RNA, VGAM2037 RNA, VGAM2038 RNA, VGAM2039 RNA, VGAM2040 RNA and VGAM2041 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4620] VGAM2036 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2036 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2036 host target RNA into VGAM2036 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4621] VGAM2037 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2037 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2037 host target RNA into VGAM2037 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4622] VGAM2038 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2038 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2038 host target RNA into VGAM2038 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4623] VGAM2039 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2039 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2039 host target RNA into VGAM2039 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4624] VGAM2040 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2040 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2040 host target RNA into VGAM2040 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4625] VGAM2041 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2041 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2041 host target RNA into VGAM2041 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4626] It is appreciated that a function of VGR3170 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3170 gene include diagnosis, prevention and treatment of viral infection by Marburg Virus. Specific functions, and accordingly utilities, of VGR3170 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3170 gene: VGAM2036 host target protein, VGAM2037 host target protein, VGAM2038 host target protein, VGAM2039 host target protein, VGAM2040 host target protein and VGAM2041 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN.

The function of these host target genes is elaborated hereinabove with reference to VGAM2036, VGAM2037, VGAM2038, VGAM2039, VGAM2040 and VGAM2041. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3171(VGR3171) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4627] VGR3171 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3171 gene was detected is described hereinabove with reference to Figs. 1-9.

[4628] VGR3171 gene encodes VGR3171 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4629] VGR3171 precursor RNA folds spatially, forming VGR3171 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3171 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3171 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4630] VGR3171 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2042 precursor RNA, VGAM2043 precursor RNA, VGAM2044 precursor RNA, VGAM2045 precursor RNA, VGAM2046 precursor RNA, VGAM2047 precursor RNA, VGAM2048 precursor RNA and VGAM2049 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4631] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2042 RNA, VGAM2043 RNA, VGAM2044 RNA, VGAM2045 RNA, VGAM2046 RNA, VGAM2047 RNA, VGAM2048 RNA and

VGAM2049 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4632] VGAM2042 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2042 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2042 host target RNA into VGAM2042 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4633] VGAM2043 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2043 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2043 host target RNA into VGAM2043 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4634] VGAM2044 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2044 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2044 host target RNA into VGAM2044 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4635] VGAM2045 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2045 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2045 host target RNA into VGAM2045 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4636] VGAM2046 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2046 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2046 host target RNA into VGAM2046 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4637] VGAM2047 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2047 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2047 host target RNA into VGAM2047 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4638] VGAM2048 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2048 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2048 host target RNA into VGAM2048 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4639] VGAM2049 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2049 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2049 host target RNA into VGAM2049 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4640] It is appreciated that a function of VGR3171 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3171 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGR3171 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3171 gene: VGAM2042 host target protein, VGAM2043 host target protein, VGAM2044 host target protein, VGAM2045 host target protein, VGAM2046 host target protein, VGAM2047 host target protein, VGAM2048 host target protein and VGAM2049 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2042, VGAM2043, VGAM2044, VGAM2045, VGAM2046, VGAM2047, VGAM2048 and VGAM2049. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3172 (VGR3172) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4641] VGR3172 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3172 gene was detected is described hereinabove with reference to Figs. 1-9.

[4642] VGR3172 gene encodes VGR3172 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4643] VGR3172 precursor RNA folds spatially, forming VGR3172 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3172 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3172 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4644] VGR3172 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2050 precursor RNA, VGAM2051 precursor RNA, VGAM2052 precursor RNA and VGAM2053 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4645] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2050 RNA, VGAM2051 RNA, VGAM2052 RNA and VGAM2053 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4646] VGAM2050 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2050 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2050 host target RNA into VGAM2050 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4647] VGAM2051 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2051 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2051 host target RNA into VGAM2051 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4648] VGAM2052 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2052 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2052 host target RNA into VGAM2052 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4649] VGAM2053 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2053 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2053 host target RNA into VGAM2053 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4650] It is appreciated that a function of VGR3172 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3172 gene include diagnosis, prevention and treatment of viral infection by Ovine Adenovirus A. Specific functions, and accordingly utilities, of VGR3172 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3172 gene: VGAM2050 host target protein, VGAM2051 host target protein, VGAM2052 host target protein and VGAM2053 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2050, VGAM2051, VGAM2052 and VGAM2053. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3173(VGR3173) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4651] VGR3173 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3173 gene was detected is described hereinabove with reference to Figs. 1-9.

[4652] VGR3173 gene encodes VGR3173 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4653] VGR3173 precursor RNA folds spatially, forming VGR3173 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3173 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3173 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4654] VGR3173 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2054 precursor RNA, VGAM2055 precursor RNA, VGAM2056 precursor RNA, VGAM2057 precursor RNA, VGAM2058 precursor RNA, VGAM2059 precursor RNA, VGAM2060 precursor RNA and VGAM2061 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4655] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2054 RNA, VGAM2055 RNA, VGAM2056 RNA, VGAM2057 RNA, VGAM2058 RNA, VGAM2059 RNA, VGAM2060 RNA and VGAM2061 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4656] VGAM2054 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2054 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2054 host target RNA into VGAM2054 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4657] VGAM2055 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2055 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2055 host target RNA into VGAM2055 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4658] VGAM2056 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2056 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2056 host target RNA into VGAM2056 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4659] VGAM2057 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2057 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2057 host target RNA into VGAM2057 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4660] VGAM2058 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2058 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2058 host target RNA into VGAM2058 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4661] VGAM2059 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2059 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2059 host target RNA into VGAM2059 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4662] VGAM2060 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2060 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2060 host target RNA into VGAM2060 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4663] VGAM2061 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2061 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2061 host target RNA into VGAM2061 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4664] It is appreciated that a function of VGR3173 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3173 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3173 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3173 gene: VGAM2054 host target protein, VGAM2055 host target protein, VGAM2056 host target protein, VGAM2057 host target protein, VGAM2058 host target protein, VGAM2059 host target protein, VGAM2060 host target protein and VGAM2061 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2054, VGAM2055, VGAM2056, VGAM2057, VGAM2058, VGAM2059, VGAM2060 and VGAM2061. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3174(VGR3174) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4665] VGR3174 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3174 gene was detected is described hereinabove with reference to Figs. 1-9.

[4666] VGR3174 gene encodes VGR3174 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4667] VGR3174 precursor RNA folds spatially, forming VGR3174 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3174 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3174 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4668] VGR3174 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2062 precursor RNA, VGAM2063 precursor RNA, VGAM2064 precursor RNA, VGAM2065 precursor RNA, VGAM2066 precursor RNA and VGAM2067 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4669] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2062 RNA, VGAM2063 RNA, VGAM2064 RNA, VGAM2065 RNA, VGAM2066 RNA and VGAM2067 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4670] VGAM2062 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2062 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2062 host target RNA into VGAM2062 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4671] VGAM2063 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2063 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2063 host target RNA into VGAM2063 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4672] VGAM2064 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2064 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2064 host target RNA into VGAM2064 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4673] VGAM2065 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2065 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2065 host target RNA into VGAM2065 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4674] VGAM2066 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2066 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2066 host target RNA into VGAM2066 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4675] VGAM2067 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2067 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2067 host target RNA into VGAM2067 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4676] It is appreciated that a function of VGR3174 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3174 gene include diagnosis, prevention and treatment of viral infection by Peanut Bud Necrosis Virus. Specific functions, and accordingly utilities, of VGR3174 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3174 gene: VGAM2062 host target protein, VGAM2063 host target protein, VGAM2064 host target protein, VGAM2065 host target protein, VGAM2066 host target protein and VGAM2067 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2062, VGAM2063, VGAM2064, VGAM2065, VGAM2066 and VGAM2067. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3175(VGR3175) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4677] VGR3175 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3175 gene was detected is described hereinabove with reference to Figs. 1–9.

[4678] VGR3175 gene encodes VGR3175 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4679] VGR3175 precursor RNA folds spatially, forming VGR3175 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3175 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3175 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4680] VGR3175 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2068 precursor RNA, VGAM2069 precursor RNA, VGAM2070 precursor RNA, VGAM2071

precursor RNA, VGAM2072 precursor RNA, VGAM2073 precursor RNA and VGAM2074 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4681] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2068 RNA, VGAM2069 RNA, VGAM2070 RNA, VGAM2071 RNA, VGAM2072 RNA, VGAM2073 RNA and VGAM2074 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4682] VGAM2068 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2068 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2068 host target RNA into VGAM2068 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4683] VGAM2069 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2069 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2069 host target RNA into VGAM2069 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4684] VGAM2070 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2070 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2070 host target RNA into VGAM2070 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4685] VGAM2071 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2071 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2071 host target RNA into VGAM2071 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4686] VGAM2072 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2072 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2072 host target RNA into VGAM2072 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4687] VGAM2073 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2073 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2073 host target RNA into VGAM2073 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4688] VGAM2074 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2074 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2074 host target RNA into VGAM2074 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4689] It is appreciated that a function of VGR3175 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3175 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3175 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3175 gene: VGAM2068 host target protein, VGAM2069 host target protein, VGAM2070 host target protein, VGAM2071 host target protein, VGAM2072 host target protein, VGAM2073 host target protein and VGAM2074 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM2068, VGAM2069, VGAM2070, VGAM2071, VGAM2072, VGAM2073 and VGAM2074. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3176(VGR3176) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4690] VGR3176 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3176 gene was detected is described hereinabove with reference to Figs. 1-9.

[4691] VGR3176 gene encodes VGR3176 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4692] VGR3176 precursor RNA folds spatially, forming VGR3176 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3176 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3176 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4693] VGR3176 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2075 precursor RNA, VGAM2076 precursor RNA, VGAM2077 precursor RNA, VGAM2078 precursor RNA, VGAM2079 precursor RNA, VGAM2080 precursor RNA, VGAM2081 precursor RNA and VGAM2082 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4694] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2075 RNA, VGAM2076 RNA, VGAM2077 RNA, VGAM2078 RNA, VGAM2079 RNA, VGAM2080 RNA, VGAM2081 RNA and

VGAM2082 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4695] VGAM2075 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2075 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2075 host target RNA into VGAM2075 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4696] VGAM2076 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2076 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2076 host target RNA into VGAM2076 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4697] VGAM2077 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2077 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2077 host target RNA into VGAM2077 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4698] VGAM2078 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2078 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2078 host target RNA into VGAM2078 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4699] VGAM2079 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2079 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2079 host target RNA into VGAM2079 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4700] VGAM2080 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2080 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2080 host target RNA into VGAM2080 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4701] VGAM2081 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2081 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2081 host target RNA into VGAM2081 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4702] VGAM2082 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2082 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2082 host target RNA into VGAM2082 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4703] It is appreciated that a function of VGR3176 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3176 gene include diagnosis, prevention and treatment of viral infection by Variola Virus. Specific functions, and accordingly utilities, of VGR3176 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3176 gene: VGAM2075 host target protein, VGAM2076 host target protein, VGAM2077 host target protein, VGAM2078 host target protein, VGAM2079 host target protein, VGAM2080 host target protein, VGAM2081 host target protein and VGAM2082 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The

function of these host target genes is elaborated herein—above with reference to VGAM2075, VGAM2076, VGAM2077, VGAM2078, VGAM2079, VGAM2080, VGAM2081 and VGAM2082. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3177(VGR3177) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4704] VGR3177 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3177 gene was detected is described hereinabove with reference to Figs. 1–9.

[4705] VGR3177 gene encodes VGR3177 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4706] VGR3177 precursor RNA folds spatially, forming VGR3177 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3177 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3177 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4707] VGR3177 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2083 precursor RNA and VGAM2084 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4708] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2083 RNA and VGAM2084 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4709] VGAM2083 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2083 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2083 host target RNA into VGAM2083 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4710] VGAM2084 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2084 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2084 host target RNA into VGAM2084 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4711] It is appreciated that a function of VGR3177 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3177 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3177 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3177 gene: VGAM2083 host target protein and VGAM2084 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2083 and VGAM2084. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3178(VGR3178) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4712] VGR3178 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3178 gene was detected is described hereinabove with reference to Figs. 1-9.

[4713] VGR3178 gene encodes VGR3178 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4714] VGR3178 precursor RNA folds spatially, forming VGR3178 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3178 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3178 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4715] VGR3178 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2085 precursor RNA, VGAM2086 precursor RNA, VGAM2087 precursor RNA, VGAM2088 precursor RNA, VGAM2089 precursor RNA, VGAM2090

precursor RNA, VGAM2091 precursor RNA and VGAM2092 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4716] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2085 RNA, VGAM2086 RNA, VGAM2087 RNA, VGAM2088 RNA, VGAM2089 RNA, VGAM2090 RNA, VGAM2091 RNA and VGAM2092 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4717] VGAM2085 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2085 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2085 host target RNA into

VGAM2085 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4718] VGAM2086 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2086 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2086 host target RNA into VGAM2086 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4719] VGAM2087 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2087 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2087 host target RNA into VGAM2087 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4720] VGAM2088 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2088 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2088 host target RNA into VGAM2088 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4721] VGAM2089 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2089 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2089 host target RNA into VGAM2089 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4722] VGAM2090 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2090 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2090 host target RNA into VGAM2090 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4723] VGAM2091 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2091 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2091 host target RNA into VGAM2091 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4724] VGAM2092 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2092 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2092 host target RNA into VGAM2092 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4725] It is appreciated that a function of VGR3178 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3178 gene include diagnosis, prevention and treatment of viral infection by

Fowlpox Virus. Specific functions, and accordingly utilities, of VGR3178 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3178 gene: VGAM2085 host target protein, VGAM2086 host target protein, VGAM2087 host target protein, VGAM2088 host target protein, VGAM2089 host target protein, VGAM2090 host target protein, VGAM2091 host target protein and VGAM2092 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2085, VGAM2086, VGAM2087, VGAM2088, VGAM2089, VGAM2090, VGAM2091 and VGAM2092. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3179(VGR3179) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4726] VGR3179 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3179 gene was detected is described hereinabove with reference to Figs. 1-9.

[4727] VGR3179 gene encodes VGR3179 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4728] VGR3179 precursor RNA folds spatially, forming VGR3179 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3179 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3179 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4729] VGR3179 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2093 precursor RNA, VGAM2094 precursor RNA, VGAM2095 precursor RNA, VGAM2096 precursor RNA, VGAM2097 precursor RNA, VGAM2098

precursor RNA, VGAM2099 precursor RNA and VGAM2100 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4730] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2093 RNA, VGAM2094 RNA, VGAM2095 RNA, VGAM2096 RNA, VGAM2097 RNA, VGAM2098 RNA, VGAM2099 RNA and VGAM2100 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4731] VGAM2093 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2093 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2093 host target RNA into

VGAM2093 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4732] VGAM2094 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2094 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2094 host target RNA into VGAM2094 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4733] VGAM2095 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2095 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2095 host target RNA into VGAM2095 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4734] VGAM2096 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2096 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2096 host target RNA into VGAM2096 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4735] VGAM2097 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2097 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2097 host target RNA into VGAM2097 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4736] VGAM2098 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2098 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2098 host target RNA into VGAM2098 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4737] VGAM2099 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2099 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2099 host target RNA into VGAM2099 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4738] VGAM2100 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2100 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2100 host target RNA into VGAM2100 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4739] It is appreciated that a function of VGR3179 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3179 gene include diagnosis, prevention and treatment of viral infection by

Camelpox Virus. Specific functions, and accordingly utilities, of VGR3179 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3179 gene: VGAM2093 host target protein, VGAM2094 host target protein, VGAM2095 host target protein, VGAM2096 host target protein, VGAM2097 host target protein, VGAM2098 host target protein, VGAM2099 host target protein and VGAM2100 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2093, VGAM2094, VGAM2095, VGAM2096, VGAM2097, VGAM2098, VGAM2099 and VGAM2100. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3180(VGR3180) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4740] VGR3180 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3180 gene was detected is described hereinabove with reference to Figs. 1-9.

[4741] VGR3180 gene encodes VGR3180 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4742] VGR3180 precursor RNA folds spatially, forming VGR3180 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3180 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3180 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4743] VGR3180 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2101 precursor RNA, VGAM2102 precursor RNA, VGAM2103 precursor RNA and VGAM2104 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4744] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2101 RNA, VGAM2102 RNA, VGAM2103 RNA and VGAM2104 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4745] VGAM2101 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2101 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2101 host target RNA into VGAM2101 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4746] VGAM2102 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2102 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2102 host target RNA into VGAM2102 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4747] VGAM2103 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2103 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2103 host target RNA into VGAM2103 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4748] VGAM2104 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2104 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2104 host target RNA into VGAM2104 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4749] It is appreciated that a function of VGR3180 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3180 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3180 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3180 gene: VGAM2101 host

target protein, VGAM2102 host target protein, VGAM2103 host target protein and VGAM2104 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM2101, VGAM2102, VGAM2103 and VGAM2104. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3181(VGR3181) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4750] VGR3181 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3181 gene was detected is described hereinabove with reference to Figs. 1–9.

[4751] VGR3181 gene encodes VGR3181 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4752] VGR3181 precursor RNA folds spatially, forming VGR3181

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3181 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3181 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4753] VGR3181 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2105 precursor RNA, VGAM2106 precursor RNA, VGAM2107 precursor RNA, VGAM2108 precursor RNA, VGAM2109 precursor RNA, VGAM2110 precursor RNA and VGAM2111 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4754] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2105 RNA, VGAM2106 RNA, VGAM2107 RNA, VGAM2108 RNA, VGAM2109 RNA, VGAM2110 RNA and VGAM2111 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4755] VGAM2105 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2105 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2105 host target RNA into VGAM2105 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4756] VGAM2106 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2106 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2106 host target RNA into VGAM2106 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4757] VGAM2107 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2107 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2107 host target RNA into VGAM2107 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4758] VGAM2108 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2108 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2108 host target RNA into VGAM2108 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4759] VGAM2109 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2109 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2109 host target RNA into VGAM2109 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4760] VGAM2110 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2110 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2110 host target RNA into VGAM2110 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4761] VGAM2111 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2111 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2111 host target RNA into VGAM2111 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4762] It is appreciated that a function of VGR3181 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3181 gene include diagnosis, prevention and treatment of viral infection by Grapevine Chrome Mosaic Virus. Specific functions, and accordingly utilities, of VGR3181 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3181 gene: VGAM2105 host target protein, VGAM2106 host target protein, VGAM2107 host target protein, VGAM2108 host target protein, VGAM2109 host target protein, VGAM2110 host target protein and VGAM2111 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2105, VGAM2106, VGAM2107, VGAM2108, VGAM2109, VGAM2110 and VGAM2111. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3182(VGR3182) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function

and utility of which at least one host target gene is known in the art.

[4763] VGR3182 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3182 gene was detected is described hereinabove with reference to Figs. 1-9.

[4764] VGR3182 gene encodes VGR3182 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4765] VGR3182 precursor RNA folds spatially, forming VGR3182 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3182 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3182 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4766] VGR3182 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM

precursor RNAs, VGAM2112 precursor RNA and VGAM2113 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4767] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2112 RNA and VGAM2113 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4768] VGAM2112 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2112 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2112 host target RNA into VGAM2112 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4769] VGAM2113 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2113 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2113 host target RNA into VGAM2113 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4770] It is appreciated that a function of VGR3182 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3182 gene include diagnosis, prevention and treatment of viral infection by Grapevine Chrome Mosaic Virus. Specific functions, and accordingly utilities, of VGR3182 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3182 gene: VGAM2112

host target protein and VGAM2113 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM2112 and VGAM2113. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3183(VGR3183) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4771] VGR3183 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3183 gene was detected is described hereinabove with reference to Figs. 1–9.

[4772] VGR3183 gene encodes VGR3183 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4773] VGR3183 precursor RNA folds spatially, forming VGR3183 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3183 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3183 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4774] VGR3183 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2114 precursor RNA, VGAM2115 precursor RNA, VGAM2116 precursor RNA, VGAM2117 precursor RNA, VGAM2118 precursor RNA, VGAM2119 precursor RNA, VGAM2120 precursor RNA and VGAM2121 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4775] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2114

RNA, VGAM2115 RNA, VGAM2116 RNA, VGAM2117 RNA, VGAM2118 RNA, VGAM2119 RNA, VGAM2120 RNA and VGAM2121 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4776] VGAM2114 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2114 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2114 host target RNA into VGAM2114 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4777] VGAM2115 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2115 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2115 host target RNA into VGAM2115 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4778] VGAM2116 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2116 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2116 host target RNA into VGAM2116 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4779] VGAM2117 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2117 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2117 host target RNA into VGAM2117 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4780] VGAM2118 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2118 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2118 host target RNA into VGAM2118 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4781] VGAM2119 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2119 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2119 host target RNA into VGAM2119 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4782] VGAM2120 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2120 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2120 host target RNA into VGAM2120 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4783] VGAM2121 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2121 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2121 host target RNA into VGAM2121 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4784] It is appreciated that a function of VGR3183 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3183 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR3183 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3183 gene: VGAM2114 host target protein, VGAM2115 host target protein, VGAM2116 host target protein, VGAM2117 host target protein, VGAM2118 host target protein, VGAM2119 host target protein, VGAM2120 host target protein and VGAM2121 host target protein,

herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM2114, VGAM2115, VGAM2116, VGAM2117, VGAM2118, VGAM2119, VGAM2120 and VGAM2121. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3184(VGR3184) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4785] VGR3184 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3184 gene was detected is described hereinabove with reference to Figs. 1–9.

[4786] VGR3184 gene encodes VGR3184 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4787] VGR3184 precursor RNA folds spatially, forming VGR3184 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3184 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3184 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4788] VGR3184 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2122 precursor RNA, VGAM2123 precursor RNA and VGAM2124 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4789] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2122 RNA, VGAM2123 RNA and VGAM2124 RNA, herein schematically represented by VGAM1 RNA through VGAM3

RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4790] VGAM2122 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2122 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2122 host target RNA into VGAM2122 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4791] VGAM2123 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2123 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2123 host target RNA into

VGAM2123 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4792] VGAM2124 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2124 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2124 host target RNA into VGAM2124 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4793] It is appreciated that a function of VGR3184 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3184 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR3184 gene correlate with, and may be deduced from, the identity of the host target genes, which are in-

hibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3184 gene: VGAM2122 host target protein, VGAM2123 host target protein and VGAM2124 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2122, VGAM2123 and VGAM2124. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3185 (VGR3185) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4794] VGR3185 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3185 gene was detected is described hereinabove with reference to Figs. 1-9.

[4795] VGR3185 gene encodes VGR3185 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4796] VGR3185 precursor RNA folds spatially, forming VGR3185 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3185 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3185 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4797] VGR3185 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2125 precursor RNA, VGAM2126 precursor RNA, VGAM2127 precursor RNA, VGAM2128 precursor RNA, VGAM2129 precursor RNA, VGAM2130 precursor RNA, VGAM2131 precursor RNA and VGAM2132 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4798] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2125 RNA, VGAM2126 RNA, VGAM2127 RNA, VGAM2128 RNA, VGAM2129 RNA, VGAM2130 RNA, VGAM2131 RNA and VGAM2132 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4799] VGAM2125 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2125 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2125 host target RNA into VGAM2125 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4800] VGAM2126 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2126 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2126 host target RNA into VGAM2126 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4801] VGAM2127 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2127 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2127 host target RNA into VGAM2127 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4802] VGAM2128 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2128 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2128 host target RNA into VGAM2128 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4803] VGAM2129 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2129 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2129 host target RNA into VGAM2129 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4804] VGAM2130 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2130 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2130 host target RNA into VGAM2130 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4805] VGAM2131 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2131 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2131 host target RNA into VGAM2131 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4806] VGAM2132 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2132 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2132 host target RNA into VGAM2132 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4807] It is appreciated that a function of VGR3185 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3185 gene include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3185 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3185 gene: VGAM2125 host target protein, VGAM2126 host target protein, VGAM2127 host target protein, VGAM2128 host target protein,

VGAM2129 host target protein, VGAM2130 host target protein, VGAM2131 host target protein and VGAM2132 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2125, VGAM2126, VGAM2127, VGAM2128, VGAM2129, VGAM2130, VGAM2131 and VGAM2132. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3186 (VGR3186) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4808] VGR3186 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3186 gene was detected is described hereinabove with reference to Figs. 1-9.

[4809] VGR3186 gene encodes VGR3186 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4810] VGR3186 precursor RNA folds spatially, forming VGR3186 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3186 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3186 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4811] VGR3186 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2133 precursor RNA, VGAM2134 precursor RNA and VGAM2135 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4812] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2133

RNA, VGAM2134 RNA and VGAM2135 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4813] VGAM2133 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2133 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2133 host target RNA into VGAM2133 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4814] VGAM2134 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2134 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2134 host target RNA into VGAM2134 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4815] VGAM2135 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2135 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2135 host target RNA into VGAM2135 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4816] It is appreciated that a function of VGR3186 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3186 gene include diagnosis, prevention and treatment of viral infection by Ateline Herpesvirus 3. Specific functions, and accordingly

utilities, of VGR3186 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3186 gene: VGAM2133 host target protein, VGAM2134 host target protein and VGAM2135 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2133, VGAM2134 and VGAM2135. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3187(VGR3187) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4817] VGR3187 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3187 gene was detected is described hereinabove with reference to Figs. 1-9.

- [4818] VGR3187 gene encodes VGR3187 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [4819] VGR3187 precursor RNA folds spatially, forming VGR3187 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3187 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3187 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [4820] VGR3187 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2136 precursor RNA, VGAM2137 precursor RNA, VGAM2138 precursor RNA, VGAM2139 precursor RNA, VGAM2140 precursor RNA, VGAM2141 precursor RNA, VGAM2142 precursor RNA and VGAM2143 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4821] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2136 RNA, VGAM2137 RNA, VGAM2138 RNA, VGAM2139 RNA, VGAM2140 RNA, VGAM2141 RNA, VGAM2142 RNA and VGAM2143 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4822] VGAM2136 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2136 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2136 host target RNA into VGAM2136 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4823] VGAM2137 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2137 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2137 host target RNA into VGAM2137 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4824] VGAM2138 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2138 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2138 host target RNA into VGAM2138 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4825] VGAM2139 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2139 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2139 host target RNA into VGAM2139 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4826] VGAM2140 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2140 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2140 host target RNA into VGAM2140 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4827] VGAM2141 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2141 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2141 host target RNA into VGAM2141 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4828] VGAM2142 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2142 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2142 host target RNA into VGAM2142 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4829] VGAM2143 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2143 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2143 host target RNA into VGAM2143 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4830] It is appreciated that a function of VGR3187 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3187 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3187 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3187 gene: VGAM2136 host target protein, VGAM2137 host target protein, VGAM2138 host target protein, VGAM2139 host target protein, VGAM2140 host target protein, VGAM2141 host target protein, VGAM2142 host target protein and VGAM2143 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2136, VGAM2137, VGAM2138, VGAM2139, VGAM2140, VGAM2141, VGAM2142 and VGAM2143. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3188(VGR3188) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4831] VGR3188 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3188 gene was detected is described hereinabove with reference to Figs. 1-9.

- [4832] VGR3188 gene encodes VGR3188 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [4833] VGR3188 precursor RNA folds spatially, forming VGR3188 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3188 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3188 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [4834] VGR3188 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2144 precursor RNA and VGAM2145 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.
- [4835] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2144 RNA and VGAM2145 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4836] VGAM2144 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2144 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2144 host target RNA into VGAM2144 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4837] VGAM2145 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2145 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2145 host target RNA into VGAM2145 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4838] It is appreciated that a function of VGR3188 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3188 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3188 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3188 gene: VGAM2144 host target protein and VGAM2145 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2144 and VGAM2145. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here

as Viral Genomic Record 3189(VGR3189) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4839] VGR3189 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3189 gene was detected is described hereinabove with reference to Figs. 1-9.

[4840] VGR3189 gene encodes VGR3189 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4841] VGR3189 precursor RNA folds spatially, forming VGR3189 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3189 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3189 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4842] VGR3189 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2146 precursor RNA, VGAM2147 precursor RNA, VGAM2148 precursor RNA, VGAM2149 precursor RNA, VGAM2150 precursor RNA, VGAM2151 precursor RNA and VGAM2152 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4843] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2146 RNA, VGAM2147 RNA, VGAM2148 RNA, VGAM2149 RNA, VGAM2150 RNA, VGAM2151 RNA and VGAM2152 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4844] VGAM2146 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2146 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2146 host target RNA into VGAM2146 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4845] VGAM2147 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2147 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2147 host target RNA into VGAM2147 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4846] VGAM2148 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2148 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2148 host target RNA into VGAM2148 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4847] VGAM2149 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2149 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2149 host target RNA into VGAM2149 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4848] VGAM2150 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2150 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2150 host target RNA into VGAM2150 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4849] VGAM2151 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2151 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2151 host target RNA into VGAM2151 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4850] VGAM2152 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2152 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2152 host target RNA into VGAM2152 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4851] It is appreciated that a function of VGR3189 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3189 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3189 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3189 gene: VGAM2146 host

target protein, VGAM2147 host target protein, VGAM2148 host target protein, VGAM2149 host target protein, VGAM2150 host target protein, VGAM2151 host target protein and VGAM2152 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2146, VGAM2147, VGAM2148, VGAM2149, VGAM2150, VGAM2151 and VGAM2152. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3190(VGR3190) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4852] VGR3190 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3190 gene was detected is described hereinabove with reference to Figs. 1-9.

[4853] VGR3190 gene encodes VGR3190 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4854] VGR3190 precursor RNA folds spatially, forming VGR3190 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3190 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3190 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4855] VGR3190 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2153 precursor RNA and VGAM2154 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4856] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2153 RNA and VGAM2154 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4857] VGAM2153 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2153 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2153 host target RNA into VGAM2153 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4858] VGAM2154 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2154 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2154 host target RNA into VGAM2154 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4859] It is appreciated that a function of VGR3190 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3190 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3190 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3190 gene: VGAM2153 host target protein and VGAM2154 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2153 and VGAM2154. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3191(VGR3191) viral gene, which

encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4860] VGR3191 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3191 gene was detected is described hereinabove with reference to Figs. 1-9.

[4861] VGR3191 gene encodes VGR3191 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4862] VGR3191 precursor RNA folds spatially, forming VGR3191 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3191 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3191 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[4863] VGR3191 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2155 precursor RNA, VGAM2156 precursor RNA, VGAM2157 precursor RNA, VGAM2158 precursor RNA, VGAM2159 precursor RNA and VGAM2160 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4864] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2155 RNA, VGAM2156 RNA, VGAM2157 RNA, VGAM2158 RNA, VGAM2159 RNA and VGAM2160 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4865] VGAM2155 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2155 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2155 host target RNA into VGAM2155 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4866] VGAM2156 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2156 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2156 host target RNA into VGAM2156 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4867] VGAM2157 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2157 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2157 host target RNA into VGAM2157 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4868] VGAM2158 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2158 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2158 host target RNA into VGAM2158 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4869] VGAM2159 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2159 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2159 host target RNA into VGAM2159 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4870] VGAM2160 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2160 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2160 host target RNA into VGAM2160 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4871] It is appreciated that a function of VGR3191 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3191 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3191 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3191 gene: VGAM2155 host target protein, VGAM2156 host target protein, VGAM2157 host target protein, VGAM2158 host target protein, VGAM2159 host target protein and VGAM2160 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2155, VGAM2156, VGAM2157, VGAM2158, VGAM2159 and VGAM2160. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3192(VGR3192) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function

and utility of which at least one host target gene is known in the art.

[4872] VGR3192 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3192 gene was detected is described hereinabove with reference to Figs. 1-9.

[4873] VGR3192 gene encodes VGR3192 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4874] VGR3192 precursor RNA folds spatially, forming VGR3192 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3192 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3192 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4875] VGR3192 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM

precursor RNAs, VGAM2161 precursor RNA, VGAM2162 precursor RNA, VGAM2163 precursor RNA, VGAM2164 precursor RNA, VGAM2165 precursor RNA, VGAM2166 precursor RNA, VGAM2167 precursor RNA and VGAM2168 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4876] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2161 RNA, VGAM2162 RNA, VGAM2163 RNA, VGAM2164 RNA, VGAM2165 RNA, VGAM2166 RNA, VGAM2167 RNA and VGAM2168 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4877] VGAM2161 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2161 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2161 host target RNA into VGAM2161 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4878] VGAM2162 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2162 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2162 host target RNA into VGAM2162 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4879] VGAM2163 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2163 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2163 host target RNA into VGAM2163 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4880] VGAM2164 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2164 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2164 host target RNA into VGAM2164 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4881] VGAM2165 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2165 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2165 host target RNA into VGAM2165 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4882] VGAM2166 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2166 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2166 host target RNA into VGAM2166 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4883] VGAM2167 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2167 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2167 host target RNA into VGAM2167 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4884] VGAM2168 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2168 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2168 host target RNA into VGAM2168 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4885] It is appreciated that a function of VGR3192 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3192 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3192 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3192 gene: VGAM2161 host target protein, VGAM2162 host target protein, VGAM2163 host target protein, VGAM2164 host target protein, VGAM2165 host target protein, VGAM2166 host target protein, VGAM2167 host target protein and VGAM2168 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2161, VGAM2162, VGAM2163, VGAM2164, VGAM2165, VGAM2166, VGAM2167 and VGAM2168. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3193(VGR3193) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of

at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4886] VGR3193 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3193 gene was detected is described hereinabove with reference to Figs. 1-9.

[4887] VGR3193 gene encodes VGR3193 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4888] VGR3193 precursor RNA folds spatially, forming VGR3193 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3193 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3193 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4889] VGR3193 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM

precursor RNAs, VGAM2169 precursor RNA, VGAM2170 precursor RNA, VGAM2171 precursor RNA, VGAM2172 precursor RNA and VGAM2173 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4890] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2169 RNA, VGAM2170 RNA, VGAM2171 RNA, VGAM2172 RNA and VGAM2173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4891] VGAM2169 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2169 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2169 host target RNA into VGAM2169 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4892] VGAM2170 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2170 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2170 host target RNA into VGAM2170 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4893] VGAM2171 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2171 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2171 host target RNA into VGAM2171 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4894] VGAM2172 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2172 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2172 host target RNA into VGAM2172 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4895] VGAM2173 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2173 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2173 host target RNA into VGAM2173 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4896] It is appreciated that a function of VGR3193 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3193 gene include diagnosis, prevention and treatment of viral infection by Camelpox Virus. Specific functions, and accordingly utilities, of VGR3193 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3193 gene: VGAM2169 host target protein, VGAM2170 host target protein, VGAM2171 host target protein, VGAM2172 host target protein and VGAM2173 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2169, VGAM2170, VGAM2171, VGAM2172

and VGAM2173. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3194(VGR3194) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4897] VGR3194 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3194 gene was detected is described hereinabove with reference to Figs. 1-9.

[4898] VGR3194 gene encodes VGR3194 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4899] VGR3194 precursor RNA folds spatially, forming VGR3194 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3194 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3194 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4900] VGR3194 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2174 precursor RNA, VGAM2175 precursor RNA, VGAM2176 precursor RNA, VGAM2177 precursor RNA, VGAM2178 precursor RNA and VGAM2179 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4901] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2174 RNA, VGAM2175 RNA, VGAM2176 RNA, VGAM2177 RNA, VGAM2178 RNA and VGAM2179 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4902] VGAM2174 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2174 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2174 host target RNA into VGAM2174 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4903] VGAM2175 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2175 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2175 host target RNA into VGAM2175 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4904] VGAM2176 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2176 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2176 host target RNA into VGAM2176 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4905] VGAM2177 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2177 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2177 host target RNA into VGAM2177 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4906] VGAM2178 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2178 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2178 host target RNA into VGAM2178 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4907] VGAM2179 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2179 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2179 host target RNA into VGAM2179 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4908] It is appreciated that a function of VGR3194 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3194 gene include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGR3194 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3194 gene: VGAM2174 host target protein, VGAM2175 host target protein, VGAM2176 host target protein, VGAM2177 host target protein, VGAM2178 host target protein and VGAM2179 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2174, VGAM2175, VGAM2176, VGAM2177, VGAM2178 and VGAM2179. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3195(VGR3195) viral

gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4909] VGR3195 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3195 gene was detected is described hereinabove with reference to Figs. 1-9.

[4910] VGR3195 gene encodes VGR3195 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4911] VGR3195 precursor RNA folds spatially, forming VGR3195 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3195 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3195 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[4912] VGR3195 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2180 precursor RNA, VGAM2181 precursor RNA, VGAM2182 precursor RNA and VGAM2183 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4913] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2180 RNA, VGAM2181 RNA, VGAM2182 RNA and VGAM2183 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4914] VGAM2180 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2180 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2180 host target RNA into VGAM2180 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4915] VGAM2181 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2181 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2181 host target RNA into VGAM2181 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4916] VGAM2182 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2182 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2182 host target RNA into VGAM2182 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4917] VGAM2183 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2183 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2183 host target RNA into VGAM2183 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4918] It is appreciated that a function of VGR3195 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3195 gene include

diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGR3195 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3195 gene: VGAM2180 host target protein, VGAM2181 host target protein, VGAM2182 host target protein and VGAM2183 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2180, VGAM2181, VGAM2182 and VGAM2183. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3196(VGR3196) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4919] VGR3196 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3196 gene was

detected is described hereinabove with reference to Figs. 1-9.

[4920] VGR3196 gene encodes VGR3196 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4921] VGR3196 precursor RNA folds spatially, forming VGR3196 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3196 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3196 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4922] VGR3196 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2184 precursor RNA, VGAM2185 precursor RNA, VGAM2186 precursor RNA, VGAM2187 precursor RNA, VGAM2188 precursor RNA, VGAM2189 precursor RNA, VGAM2190 precursor RNA and VGAM2191 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4923] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2184 RNA, VGAM2185 RNA, VGAM2186 RNA, VGAM2187 RNA, VGAM2188 RNA, VGAM2189 RNA, VGAM2190 RNA and VGAM2191 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4924] VGAM2184 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2184 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2184 host target RNA into VGAM2184 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4925] VGAM2185 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2185 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2185 host target RNA into VGAM2185 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4926] VGAM2186 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2186 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2186 host target RNA into VGAM2186 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4927] VGAM2187 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2187 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2187 host target RNA into VGAM2187 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4928] VGAM2188 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2188 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2188 host target RNA into

VGAM2188 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4929] VGAM2189 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2189 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2189 host target RNA into VGAM2189 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4930] VGAM2190 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2190 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2190 host target RNA into VGAM2190 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4931] VGAM2191 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2191 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2191 host target RNA into VGAM2191 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4932] It is appreciated that a function of VGR3196 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3196 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3196 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3196 gene: VGAM2184 host target protein, VGAM2185 host target protein, VGAM2186 host target protein, VGAM2187 host target protein, VGAM2188 host target protein, VGAM2189 host target protein, VGAM2190 host target protein and VGAM2191 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2184, VGAM2185, VGAM2186, VGAM2187, VGAM2188, VGAM2189, VGAM2190 and VGAM2191. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3197(VGR3197) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4933] VGR3197 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3197 gene was

detected is described hereinabove with reference to Figs. 1-9.

[4934] VGR3197 gene encodes VGR3197 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4935] VGR3197 precursor RNA folds spatially, forming VGR3197 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3197 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3197 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4936] VGR3197 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2192 precursor RNA, VGAM2193 precursor RNA and VGAM2194 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4937] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2192 RNA, VGAM2193 RNA and VGAM2194 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4938] VGAM2192 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2192 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2192 host target RNA into VGAM2192 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4939] VGAM2193 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2193 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2193 host target RNA into VGAM2193 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4940] VGAM2194 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2194 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2194 host target RNA into VGAM2194 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4941] It is appreciated that a function of VGR3197 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3197 gene include diagnosis, prevention and treatment of viral infection by Monkeypox Virus. Specific functions, and accordingly utilities, of VGR3197 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3197 gene: VGAM2192 host target protein, VGAM2193 host target protein and VGAM2194 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2192, VGAM2193 and VGAM2194. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3198(VGR3198) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4942] VGR3198 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3198 gene was detected is described hereinabove with reference to Figs. 1–9.

[4943] VGR3198 gene encodes VGR3198 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4944] VGR3198 precursor RNA folds spatially, forming VGR3198 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3198 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3198 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[4945] VGR3198 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2195 precursor RNA, VGAM2196 precursor RNA, VGAM2197 precursor RNA, VGAM2198

precursor RNA and VGAM2199 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4946] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2195 RNA, VGAM2196 RNA, VGAM2197 RNA, VGAM2198 RNA and VGAM2199 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4947] VGAM2195 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2195 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2195 host target RNA into VGAM2195 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4948] VGAM2196 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2196 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2196 host target RNA into VGAM2196 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4949] VGAM2197 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2197 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2197 host target RNA into

VGAM2197 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4950] VGAM2198 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2198 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2198 host target RNA into VGAM2198 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4951] VGAM2199 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2199 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2199 host target RNA into VGAM2199 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4952] It is appreciated that a function of VGR3198 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3198 gene include diagnosis, prevention and treatment of viral infection by Yaba-like Disease Virus. Specific functions, and accordingly utilities, of VGR3198 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3198 gene: VGAM2195 host target protein, VGAM2196 host target protein, VGAM2197 host target protein, VGAM2198 host target protein and VGAM2199 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2195, VGAM2196, VGAM2197, VGAM2198 and VGAM2199. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory vi-

ral gene, referred to here as Viral Genomic Record 3199(VGR3199) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4953] VGR3199 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3199 gene was detected is described hereinabove with reference to Figs. 1-9.

[4954] VGR3199 gene encodes VGR3199 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4955] VGR3199 precursor RNA folds spatially, forming VGR3199 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3199 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3199 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[4956] VGR3199 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2200 precursor RNA, VGAM2201 precursor RNA, VGAM2202 precursor RNA, VGAM2203 precursor RNA, VGAM2204 precursor RNA, VGAM2205 precursor RNA and VGAM2206 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4957] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2200 RNA, VGAM2201 RNA, VGAM2202 RNA, VGAM2203 RNA, VGAM2204 RNA, VGAM2205 RNA and VGAM2206 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4958] VGAM2200 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2200 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2200 host target RNA into VGAM2200 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4959] VGAM2201 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2201 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2201 host target RNA into VGAM2201 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4960] VGAM2202 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2202 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2202 host target RNA into VGAM2202 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4961] VGAM2203 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2203 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2203 host target RNA into VGAM2203 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4962] VGAM2204 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2204 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2204 host target RNA into VGAM2204 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4963] VGAM2205 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2205 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2205 host target RNA into VGAM2205 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4964] VGAM2206 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2206 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2206 host target RNA into VGAM2206 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4965] It is appreciated that a function of VGR3199 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3199 gene include diagnosis, prevention and treatment of viral infection by Cowpox Virus. Specific functions, and accordingly utilities, of VGR3199 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3199 gene: VGAM2200 host target protein,

VGAM2201 host target protein, VGAM2202 host target protein, VGAM2203 host target protein, VGAM2204 host target protein, VGAM2205 host target protein and VGAM2206 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2200, VGAM2201, VGAM2202, VGAM2203, VGAM2204, VGAM2205 and VGAM2206. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3200 (VGR3200) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4966] VGR3200 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3200 gene was detected is described hereinabove with reference to Figs. 1-9.

[4967] VGR3200 gene encodes VGR3200 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[4968] VGR3200 precursor RNA folds spatially, forming VGR3200 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3200 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3200 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4969] VGR3200 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2207 precursor RNA, VGAM2208 precursor RNA, VGAM2209 precursor RNA, VGAM2210 precursor RNA, VGAM2211 precursor RNA, VGAM2212 precursor RNA, VGAM2213 precursor RNA and VGAM2214 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4970] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2207 RNA, VGAM2208 RNA, VGAM2209 RNA, VGAM2210 RNA, VGAM2211 RNA, VGAM2212 RNA, VGAM2213 RNA and VGAM2214 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4971] VGAM2207 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2207 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2207 host target RNA into VGAM2207 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4972] VGAM2208 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2208 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2208 host target RNA into VGAM2208 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4973] VGAM2209 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2209 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2209 host target RNA into VGAM2209 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4974] VGAM2210 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2210 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2210 host target RNA into VGAM2210 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4975] VGAM2211 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2211 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2211 host target RNA into VGAM2211 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4976] VGAM2212 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2212 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2212 host target RNA into VGAM2212 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4977] VGAM2213 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2213 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2213 host target RNA into VGAM2213 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4978] VGAM2214 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2214 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2214 host target RNA into VGAM2214 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4979] It is appreciated that a function of VGR3200 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3200 gene include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGR3200 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3200 gene: VGAM2207 host target protein, VGAM2208 host target protein, VGAM2209

host target protein, VGAM2210 host target protein, VGAM2211 host target protein, VGAM2212 host target protein, VGAM2213 host target protein and VGAM2214 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2207, VGAM2208, VGAM2209, VGAM2210, VGAM2211, VGAM2212, VGAM2213 and VGAM2214. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3201 (VGR3201) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4980] VGR3201 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3201 gene was detected is described hereinabove with reference to Figs. 1-9.

[4981] VGR3201 gene encodes VGR3201 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[4982] VGR3201 precursor RNA folds spatially, forming VGR3201 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3201 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3201 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4983] VGR3201 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2215 precursor RNA, VGAM2216 precursor RNA, VGAM2217 precursor RNA, VGAM2218 precursor RNA, VGAM2219 precursor RNA and VGAM2220 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4984] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2215 RNA, VGAM2216 RNA, VGAM2217 RNA, VGAM2218 RNA, VGAM2219 RNA and VGAM2220 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4985] VGAM2215 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2215 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2215 host target RNA into VGAM2215 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4986] VGAM2216 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2216 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2216 host target RNA into VGAM2216 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4987] VGAM2217 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2217 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2217 host target RNA into VGAM2217 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4988] VGAM2218 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2218 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2218 host target RNA into VGAM2218 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4989] VGAM2219 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2219 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2219 host target RNA into VGAM2219 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4990] VGAM2220 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2220 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2220 host target RNA into VGAM2220 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4991] It is appreciated that a function of VGR3201 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3201 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3201 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3201 gene: VGAM2215 host target protein, VGAM2216 host target protein, VGAM2217 host target protein, VGAM2218 host target protein, VGAM2219 host target protein and VGAM2220 host target

protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2215, VGAM2216, VGAM2217, VGAM2218, VGAM2219 and VGAM2220. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3202(VGR3202) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[4992] VGR3202 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3202 gene was detected is described hereinabove with reference to Figs. 1-9.

[4993] VGR3202 gene encodes VGR3202 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[4994] VGR3202 precursor RNA folds spatially, forming VGR3202 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3202 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3202 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[4995] VGR3202 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2221 precursor RNA, VGAM2222 precursor RNA, VGAM2223 precursor RNA, VGAM2224 precursor RNA, VGAM2225 precursor RNA, VGAM2226 precursor RNA, VGAM2227 precursor RNA and VGAM2228 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[4996] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2221

RNA, VGAM2222 RNA, VGAM2223 RNA, VGAM2224 RNA, VGAM2225 RNA, VGAM2226 RNA, VGAM2227 RNA and VGAM2228 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[4997] VGAM2221 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2221 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2221 host target RNA into VGAM2221 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4998] VGAM2222 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2222 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2222 host target RNA into VGAM2222 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[4999] VGAM2223 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2223 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2223 host target RNA into VGAM2223 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5000] VGAM2224 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2224 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2224 host target RNA into VGAM2224 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5001] VGAM2225 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2225 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2225 host target RNA into VGAM2225 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5002] VGAM2226 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2226 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2226 host target RNA into VGAM2226 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5003] VGAM2227 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2227 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2227 host target RNA into VGAM2227 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5004] VGAM2228 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2228 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2228 host target RNA into VGAM2228 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5005] It is appreciated that a function of VGR3202 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3202 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3202 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3202 gene: VGAM2221 host target protein, VGAM2222 host target protein, VGAM2223 host target protein, VGAM2224 host target protein, VGAM2225 host target protein, VGAM2226 host target protein, VGAM2227 host target protein and VGAM2228

host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2221, VGAM2222, VGAM2223, VGAM2224, VGAM2225, VGAM2226, VGAM2227 and VGAM2228. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3203 (VGR3203) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5006] VGR3203 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3203 gene was detected is described hereinabove with reference to Figs. 1-9.

[5007] VGR3203 gene encodes VGR3203 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5008] VGR3203 precursor RNA folds spatially, forming VGR3203 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3203 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3203 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5009] VGR3203 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2229 precursor RNA, VGAM2230 precursor RNA and VGAM2231 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5010] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2229 RNA, VGAM2230 RNA and VGAM2231 RNA, herein schematically represented by VGAM1 RNA through VGAM3

RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5011] VGAM2229 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2229 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2229 host target RNA into VGAM2229 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5012] VGAM2230 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2230 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2230 host target RNA into

VGAM2230 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5013] VGAM2231 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2231 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2231 host target RNA into VGAM2231 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5014] It is appreciated that a function of VGR3203 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3203 gene include diagnosis, prevention and treatment of viral infection by Potato Aucuba Mosaic Virus. Specific functions, and accordingly utilities, of VGR3203 gene correlate with, and may be deduced from, the identity of the host target

genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3203 gene: VGAM2229 host target protein, VGAM2230 host target protein and VGAM2231 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2229, VGAM2230 and VGAM2231. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3204(VGR3204) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5015] VGR3204 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3204 gene was detected is described hereinabove with reference to Figs. 1-9.

[5016] VGR3204 gene encodes VGR3204 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[5017] VGR3204 precursor RNA folds spatially, forming VGR3204 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3204 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3204 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5018] VGR3204 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2232 precursor RNA, VGAM2233 precursor RNA, VGAM2234 precursor RNA, VGAM2235 precursor RNA, VGAM2236 precursor RNA, VGAM2237 precursor RNA, VGAM2238 precursor RNA and VGAM2239 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5019] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2232 RNA, VGAM2233 RNA, VGAM2234 RNA, VGAM2235 RNA, VGAM2236 RNA, VGAM2237 RNA, VGAM2238 RNA and VGAM2239 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5020] VGAM2232 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2232 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2232 host target RNA into VGAM2232 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5021] VGAM2233 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2233 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2233 host target RNA into VGAM2233 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5022] VGAM2234 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2234 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2234 host target RNA into VGAM2234 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5023] VGAM2235 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2235 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2235 host target RNA into VGAM2235 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5024] VGAM2236 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2236 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2236 host target RNA into VGAM2236 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5025] VGAM2237 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2237 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2237 host target RNA into VGAM2237 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5026] VGAM2238 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2238 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2238 host target RNA into VGAM2238 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5027] VGAM2239 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2239 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2239 host target RNA into VGAM2239 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5028] It is appreciated that a function of VGR3204 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3204 gene include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGR3204 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3204 gene: VGAM2232 host target protein, VGAM2233 host target protein,

VGAM2234 host target protein, VGAM2235 host target protein, VGAM2236 host target protein, VGAM2237 host target protein, VGAM2238 host target protein and VGAM2239 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2232, VGAM2233, VGAM2234, VGAM2235, VGAM2236, VGAM2237, VGAM2238 and VGAM2239. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3205(VGR3205) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5029] VGR3205 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3205 gene was detected is described hereinabove with reference to Figs. 1-9.

[5030] VGR3205 gene encodes VGR3205 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5031] VGR3205 precursor RNA folds spatially, forming VGR3205 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3205 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3205 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5032] VGR3205 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2240 precursor RNA, VGAM2241 precursor RNA, VGAM2242 precursor RNA, VGAM2243 precursor RNA, VGAM2244 precursor RNA, VGAM2245 precursor RNA and VGAM2246 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[5033] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2240 RNA, VGAM2241 RNA, VGAM2242 RNA, VGAM2243 RNA, VGAM2244 RNA, VGAM2245 RNA and VGAM2246 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5034] VGAM2240 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2240 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2240 host target RNA into VGAM2240 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5035] VGAM2241 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2241 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2241 host target RNA into VGAM2241 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5036] VGAM2242 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2242 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2242 host target RNA into VGAM2242 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5037] VGAM2243 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2243 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2243 host target RNA into VGAM2243 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5038] VGAM2244 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2244 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2244 host target RNA into VGAM2244 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5039] VGAM2245 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2245 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2245 host target RNA into VGAM2245 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5040] VGAM2246 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2246 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2246 host target RNA into VGAM2246 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5041] It is appreciated that a function of VGR3205 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3205 gene include diagnosis, prevention and treatment of viral infection by Porcine Epidemic Diarrhea Virus. Specific functions, and accordingly utilities, of VGR3205 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3205 gene: VGAM2240 host target protein, VGAM2241 host target protein, VGAM2242 host target protein, VGAM2243 host target protein, VGAM2244 host target protein, VGAM2245 host target protein and VGAM2246 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2240, VGAM2241, VGAM2242, VGAM2243, VGAM2244, VGAM2245 and VGAM2246. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3206(VGR3206) viral

gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5042] VGR3206 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3206 gene was detected is described hereinabove with reference to Figs. 1-9.

[5043] VGR3206 gene encodes VGR3206 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5044] VGR3206 precursor RNA folds spatially, forming VGR3206 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3206 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3206 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[5045] VGR3206 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2247 precursor RNA, VGAM2248 precursor RNA, VGAM2249 precursor RNA, VGAM2250 precursor RNA, VGAM2251 precursor RNA, VGAM2252 precursor RNA and VGAM2253 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5046] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2247 RNA, VGAM2248 RNA, VGAM2249 RNA, VGAM2250 RNA, VGAM2251 RNA, VGAM2252 RNA and VGAM2253 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5047] VGAM2247 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2247 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2247 host target RNA into VGAM2247 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5048] VGAM2248 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2248 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2248 host target RNA into VGAM2248 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5049] VGAM2249 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2249 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2249 host target RNA into VGAM2249 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5050] VGAM2250 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2250 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2250 host target RNA into VGAM2250 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5051] VGAM2251 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2251 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2251 host target RNA into VGAM2251 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5052] VGAM2252 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2252 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2252 host target RNA into VGAM2252 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5053] VGAM2253 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2253 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2253 host target RNA into VGAM2253 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5054] It is appreciated that a function of VGR3206 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3206 gene include diagnosis, prevention and treatment of viral infection by Transmissible Gastroenteritis Virus. Specific functions, and accordingly utilities, of VGR3206 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3206 gene: VGAM2247 host target protein, VGAM2248 host target protein,

VGAM2249 host target protein, VGAM2250 host target protein, VGAM2251 host target protein, VGAM2252 host target protein and VGAM2253 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2247, VGAM2248, VGAM2249, VGAM2250, VGAM2251, VGAM2252 and VGAM2253. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3207(VGR3207) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5055] VGR3207 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3207 gene was detected is described hereinabove with reference to Figs. 1-9.

[5056] VGR3207 gene encodes VGR3207 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[5057] VGR3207 precursor RNA folds spatially, forming VGR3207 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3207 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3207 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5058] VGR3207 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2254 precursor RNA and VGAM2255 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5059] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2254

RNA and VGAM2255 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5060] VGAM2254 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2254 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2254 host target RNA into VGAM2254 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5061] VGAM2255 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2255 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2255 host target RNA into VGAM2255 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5062] It is appreciated that a function of VGR3207 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3207 gene include diagnosis, prevention and treatment of viral infection by Transmissible Gastroenteritis Virus. Specific functions, and accordingly utilities, of VGR3207 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3207 gene: VGAM2254 host target protein and VGAM2255 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2254 and VGAM2255. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3208(VGR3208) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5063] VGR3208 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3208 gene was detected is described hereinabove with reference to Figs. 1-9.

[5064] VGR3208 gene encodes VGR3208 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5065] VGR3208 precursor RNA folds spatially, forming VGR3208 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3208 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3208 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5066] VGR3208 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2256 precursor RNA, VGAM2257 precursor RNA and VGAM2258 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5067] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2256 RNA, VGAM2257 RNA and VGAM2258 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5068] VGAM2256 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2256 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2256 host target RNA into VGAM2256 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5069] VGAM2257 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2257 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2257 host target RNA into VGAM2257 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5070] VGAM2258 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2258 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2258 host target RNA into VGAM2258 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5071] It is appreciated that a function of VGR3208 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3208 gene include diagnosis, prevention and treatment of viral infection by Oat Chlorotic Stunt Virus. Specific functions, and accordingly utilities, of VGR3208 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3208 gene: VGAM2256 host target protein, VGAM2257 host target protein and VGAM2258 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2256, VGAM2257 and VGAM2258. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 3209(VGR3209) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5072] VGR3209 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3209 gene was detected is described hereinabove with reference to Figs. 1-9.

[5073] VGR3209 gene encodes VGR3209 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5074] VGR3209 precursor RNA folds spatially, forming VGR3209 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3209 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3209 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5075] VGR3209 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2259 precursor RNA, VGAM2260 precursor RNA, VGAM2261 precursor RNA, VGAM2262 precursor RNA, VGAM2263 precursor RNA, VGAM2264 precursor RNA, VGAM2265 precursor RNA and VGAM2266 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5076] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2259 RNA, VGAM2260 RNA, VGAM2261 RNA, VGAM2262 RNA, VGAM2263 RNA, VGAM2264 RNA, VGAM2265 RNA and VGAM2266 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5077] VGAM2259 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2259 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2259 host target RNA into VGAM2259 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5078] VGAM2260 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2260 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2260 host target RNA into VGAM2260 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5079] VGAM2261 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2261 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2261 host target RNA into VGAM2261 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5080] VGAM2262 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2262 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2262 host target RNA into VGAM2262 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5081] VGAM2263 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2263 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2263 host target RNA into VGAM2263 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5082] VGAM2264 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2264 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2264 host target RNA into VGAM2264 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5083] VGAM2265 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2265 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2265 host target RNA into VGAM2265 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5084] VGAM2266 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2266 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2266 host target RNA into

VGAM2266 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5085] It is appreciated that a function of VGR3209 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3209 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3209 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3209 gene: VGAM2259 host target protein, VGAM2260 host target protein, VGAM2261 host target protein, VGAM2262 host target protein, VGAM2263 host target protein, VGAM2264 host target protein, VGAM2265 host target protein and VGAM2266 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2259, VGAM2260, VGAM2261, VGAM2262, VGAM2263, VGAM2264, VGAM2265 and VGAM2266. Fig. 9 further

provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3210(VGR3210) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5086] VGR3210 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3210 gene was detected is described hereinabove with reference to Figs. 1-9.

[5087] VGR3210 gene encodes VGR3210 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5088] VGR3210 precursor RNA folds spatially, forming VGR3210 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3210 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3210 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5089] VGR3210 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2267 precursor RNA, VGAM2268 precursor RNA, VGAM2269 precursor RNA, VGAM2270 precursor RNA, VGAM2271 precursor RNA, VGAM2272 precursor RNA, VGAM2273 precursor RNA and VGAM2274 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5090] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2267 RNA, VGAM2268 RNA, VGAM2269 RNA, VGAM2270 RNA, VGAM2271 RNA, VGAM2272 RNA, VGAM2273 RNA and VGAM2274 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5091] VGAM2267 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2267 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2267 host target RNA into VGAM2267 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5092] VGAM2268 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2268 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2268 host target RNA into VGAM2268 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5093] VGAM2269 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2269 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2269 host target RNA into VGAM2269 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5094] VGAM2270 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2270 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2270 host target RNA into VGAM2270 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5095] VGAM2271 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2271 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2271 host target RNA into VGAM2271 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5096] VGAM2272 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2272 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2272 host target RNA into VGAM2272 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5097] VGAM2273 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2273 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2273 host target RNA into VGAM2273 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5098] VGAM2274 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2274 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2274 host target RNA into

VGAM2274 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5099] It is appreciated that a function of VGR3210 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3210 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3210 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3210 gene: VGAM2267 host target protein, VGAM2268 host target protein, VGAM2269 host target protein, VGAM2270 host target protein, VGAM2271 host target protein, VGAM2272 host target protein, VGAM2273 host target protein and VGAM2274 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2267, VGAM2268, VGAM2269, VGAM2270, VGAM2271, VGAM2272, VGAM2273 and VGAM2274. Fig. 9 further

provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3211(VGR3211) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5100] VGR3211 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3211 gene was detected is described hereinabove with reference to Figs. 1-9.

[5101] VGR3211 gene encodes VGR3211 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5102] VGR3211 precursor RNA folds spatially, forming VGR3211 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3211 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3211 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5103] VGR3211 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2275 precursor RNA, VGAM2276 precursor RNA, VGAM2277 precursor RNA, VGAM2278 precursor RNA, VGAM2279 precursor RNA and VGAM2280 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5104] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2275 RNA, VGAM2276 RNA, VGAM2277 RNA, VGAM2278 RNA, VGAM2279 RNA and VGAM2280 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5105] VGAM2275 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2275 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2275 host target RNA into VGAM2275 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5106] VGAM2276 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2276 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2276 host target RNA into VGAM2276 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5107] VGAM2277 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2277 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2277 host target RNA into VGAM2277 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5108] VGAM2278 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2278 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2278 host target RNA into VGAM2278 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5109] VGAM2279 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2279 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2279 host target RNA into VGAM2279 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5110] VGAM2280 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2280 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2280 host target RNA into VGAM2280 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5111] It is appreciated that a function of VGR3211 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3211 gene include diagnosis, prevention and treatment of viral infection by Alcelaphine Herpesvirus 1. Specific functions, and accordingly utilities, of VGR3211 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3211 gene: VGAM2275 host target protein, VGAM2276 host target protein, VGAM2277 host target protein, VGAM2278 host target protein, VGAM2279 host target protein and VGAM2280 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2275, VGAM2276, VGAM2277, VGAM2278, VGAM2279 and VGAM2280. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3212(VGR3212) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates

expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5112] VGR3212 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3212 gene was detected is described hereinabove with reference to Figs. 1-9.

[5113] VGR3212 gene encodes VGR3212 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5114] VGR3212 precursor RNA folds spatially, forming VGR3212 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3212 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3212 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5115] VGR3212 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2281 precursor RNA, VGAM2282 precursor RNA, VGAM2283 precursor RNA, VGAM2284 precursor RNA, VGAM2285 precursor RNA, VGAM2286 precursor RNA, VGAM2287 precursor RNA and VGAM2288 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5116] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2281 RNA, VGAM2282 RNA, VGAM2283 RNA, VGAM2284 RNA, VGAM2285 RNA, VGAM2286 RNA, VGAM2287 RNA and VGAM2288 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5117] VGAM2281 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2281 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2281 host target RNA into VGAM2281 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5118] VGAM2282 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2282 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2282 host target RNA into VGAM2282 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5119] VGAM2283 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2283 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2283 host target RNA into VGAM2283 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5120] VGAM2284 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2284 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2284 host target RNA into VGAM2284 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5121] VGAM2285 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2285 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2285 host target RNA into VGAM2285 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5122] VGAM2286 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2286 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2286 host target RNA into VGAM2286 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5123] VGAM2287 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2287 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2287 host target RNA into VGAM2287 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5124] VGAM2288 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2288 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2288 host target RNA into VGAM2288 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5125] It is appreciated that a function of VGR3212 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3212 gene include diagnosis, prevention and treatment of viral infection by Murine Hepatitis Virus. Specific functions, and accordingly utilities, of VGR3212 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3212 gene: VGAM2281 host target protein, VGAM2282 host target protein, VGAM2283 host target protein, VGAM2284 host target protein, VGAM2285 host target protein, VGAM2286 host target protein, VGAM2287 host target protein and VGAM2288 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2281, VGAM2282, VGAM2283, VGAM2284, VGAM2285, VGAM2286, VGAM2287 and VGAM2288. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3213(VGR3213) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-

like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5126] VGR3213 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3213 gene was detected is described hereinabove with reference to Figs. 1-9.

[5127] VGR3213 gene encodes VGR3213 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5128] VGR3213 precursor RNA folds spatially, forming VGR3213 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3213 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3213 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5129] VGR3213 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2289 precursor RNA, VGAM2290 precursor RNA, VGAM2291 precursor RNA, VGAM2292 precursor RNA, VGAM2293 precursor RNA and VGAM2294 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5130] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2289 RNA, VGAM2290 RNA, VGAM2291 RNA, VGAM2292 RNA, VGAM2293 RNA and VGAM2294 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5131] VGAM2289 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2289 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2289 host target RNA into VGAM2289 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5132] VGAM2290 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2290 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2290 host target RNA into VGAM2290 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5133] VGAM2291 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2291 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2291 host target RNA into VGAM2291 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5134] VGAM2292 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2292 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2292 host target RNA into VGAM2292 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5135] VGAM2293 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2293 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2293 host target RNA into VGAM2293 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5136] VGAM2294 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2294 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2294 host target RNA into VGAM2294 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5137] It is appreciated that a function of VGR3213 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3213 gene include diagnosis, prevention and treatment of viral infection by Murine Hepatitis Virus. Specific functions, and accordingly utilities, of VGR3213 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3213 gene: VGAM2289 host target protein, VGAM2290 host target protein, VGAM2291 host target protein, VGAM2292 host target protein, VGAM2293 host target protein and VGAM2294 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2289, VGAM2290, VGAM2291, VGAM2292, VGAM2293 and VGAM2294. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3214(VGR3214) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5138] VGR3214 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3214 gene was detected is described hereinabove with reference to Figs. 1-9.

[5139] VGR3214 gene encodes VGR3214 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5140] VGR3214 precursor RNA folds spatially, forming VGR3214 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3214 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3214 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5141] VGR3214 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2295 precursor RNA, VGAM2296 precursor RNA, VGAM2297 precursor RNA, VGAM2298

precursor RNA, VGAM2299 precursor RNA, VGAM2300 precursor RNA, VGAM2301 precursor RNA and VGAM2302 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5142] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2295 RNA, VGAM2296 RNA, VGAM2297 RNA, VGAM2298 RNA, VGAM2299 RNA, VGAM2300 RNA, VGAM2301 RNA and VGAM2302 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5143] VGAM2295 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2295 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2295 host target RNA into VGAM2295 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5144] VGAM2296 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2296 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2296 host target RNA into VGAM2296 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5145] VGAM2297 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2297 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2297 host target RNA into VGAM2297 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5146] VGAM2298 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2298 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2298 host target RNA into VGAM2298 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5147] VGAM2299 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2299 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2299 host target RNA into VGAM2299 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5148] VGAM2300 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2300 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2300 host target RNA into VGAM2300 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5149] VGAM2301 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2301 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2301 host target RNA into VGAM2301 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5150] VGAM2302 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2302 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2302 host target RNA into VGAM2302 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5151] It is appreciated that a function of VGR3214 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3214 gene include

diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3214 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3214 gene: VGAM2295 host target protein, VGAM2296 host target protein, VGAM2297 host target protein, VGAM2298 host target protein, VGAM2299 host target protein, VGAM2300 host target protein, VGAM2301 host target protein and VGAM2302 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2295, VGAM2296, VGAM2297, VGAM2298, VGAM2299, VGAM2300, VGAM2301 and VGAM2302. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3215(VGR3215) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5152] VGR3215 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3215 gene was detected is described hereinabove with reference to Figs. 1-9.

[5153] VGR3215 gene encodes VGR3215 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5154] VGR3215 precursor RNA folds spatially, forming VGR3215 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3215 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3215 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5155] VGR3215 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2303 precursor RNA, VGAM2304 precursor RNA, VGAM2305 precursor RNA and VGAM2306

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5156] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2303 RNA, VGAM2304 RNA, VGAM2305 RNA and VGAM2306 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5157] VGAM2303 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2303 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2303 host target RNA into VGAM2303 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5158] VGAM2304 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2304 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2304 host target RNA into VGAM2304 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5159] VGAM2305 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2305 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2305 host target RNA into VGAM2305 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5160] VGAM2306 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2306 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2306 host target RNA into VGAM2306 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5161] It is appreciated that a function of VGR3215 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3215 gene include diagnosis, prevention and treatment of viral infection by Ectromelia Virus. Specific functions, and accordingly utilities, of VGR3215 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3215 gene: VGAM2303 host target protein, VGAM2304 host target protein, VGAM2305 host target protein and VGAM2306 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2303, VGAM2304, VGAM2305 and VGAM2306. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3216(VGR3216) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5162] VGR3216 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3216 gene was detected is described hereinabove with reference to Figs. 1-9.

[5163] VGR3216 gene encodes VGR3216 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5164] VGR3216 precursor RNA folds spatially, forming VGR3216 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3216 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3216 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5165] VGR3216 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2307 precursor RNA, VGAM2308 precursor RNA, VGAM2309 precursor RNA, VGAM2310 precursor RNA, VGAM2311 precursor RNA, VGAM2312 precursor RNA and VGAM2313 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5166] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2307 RNA, VGAM2308 RNA, VGAM2309 RNA, VGAM2310 RNA, VGAM2311 RNA, VGAM2312 RNA and VGAM2313 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5167] VGAM2307 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2307 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2307 host target RNA into VGAM2307 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5168] VGAM2308 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2308 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2308 host target RNA into VGAM2308 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5169] VGAM2309 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2309 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2309 host target RNA into VGAM2309 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5170] VGAM2310 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2310 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2310 host target RNA into VGAM2310 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5171] VGAM2311 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2311 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2311 host target RNA into VGAM2311 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5172] VGAM2312 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2312 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2312 host target RNA into VGAM2312 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5173] VGAM2313 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2313 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2313 host target RNA into VGAM2313 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5174] It is appreciated that a function of VGR3216 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3216 gene include diagnosis, prevention and treatment of viral infection by Lumpy Skin Disease Virus. Specific functions, and accordingly utilities, of VGR3216 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3216 gene: VGAM2307 host target protein, VGAM2308 host target protein, VGAM2309 host target protein, VGAM2310 host target protein, VGAM2311 host target protein, VGAM2312 host target protein and VGAM2313 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2307, VGAM2308, VGAM2309, VGAM2310, VGAM2311, VGAM2312 and VGAM2313. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3217(VGR3217) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates

expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5175] VGR3217 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3217 gene was detected is described hereinabove with reference to Figs. 1-9.

[5176] VGR3217 gene encodes VGR3217 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5177] VGR3217 precursor RNA folds spatially, forming VGR3217 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3217 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3217 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5178] VGR3217 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2314 precursor RNA and VGAM2315 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5179] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2314 RNA and VGAM2315 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5180] VGAM2314 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2314 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2314 host target RNA into VGAM2314 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5181] VGAM2315 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2315 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2315 host target RNA into VGAM2315 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5182] It is appreciated that a function of VGR3217 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3217 gene include diagnosis, prevention and treatment of viral infection by Lumpy Skin Disease Virus. Specific functions, and accordingly utilities, of VGR3217 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the

`operon-like` cluster of VGR3217 gene: VGAM2314 host target protein and VGAM2315 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2314 and VGAM2315. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3218(VGR3218) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5183] VGR3218 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3218 gene was detected is described hereinabove with reference to Figs. 1-9.

[5184] VGR3218 gene encodes VGR3218 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5185] VGR3218 precursor RNA folds spatially, forming VGR3218

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3218 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3218 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5186] VGR3218 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2316 precursor RNA, VGAM2317 precursor RNA, VGAM2318 precursor RNA, VGAM2319 precursor RNA, VGAM2320 precursor RNA, VGAM2321 precursor RNA, VGAM2322 precursor RNA and VGAM2323 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5187] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2316 RNA, VGAM2317 RNA, VGAM2318 RNA, VGAM2319 RNA, VGAM2320 RNA, VGAM2321 RNA, VGAM2322 RNA and VGAM2323 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5188] VGAM2316 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2316 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2316 host target RNA into VGAM2316 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5189] VGAM2317 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2317 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2317 host target RNA into VGAM2317 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5190] VGAM2318 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2318 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2318 host target RNA into VGAM2318 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5191] VGAM2319 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2319 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2319 host target RNA into VGAM2319 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5192] VGAM2320 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2320 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2320 host target RNA into VGAM2320 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5193] VGAM2321 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2321 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2321 host target RNA into VGAM2321 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5194] VGAM2322 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2322 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2322 host target RNA into VGAM2322 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5195] VGAM2323 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2323 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2323 host target RNA into VGAM2323 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5196] It is appreciated that a function of VGR3218 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3218 gene include diagnosis, prevention and treatment of viral infection by Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3218 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3218 gene: VGAM2316 host target protein, VGAM2317 host target protein, VGAM2318 host target protein, VGAM2319 host target protein, VGAM2320 host target protein, VGAM2321 host target

protein, VGAM2322 host target protein and VGAM2323 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2316, VGAM2317, VGAM2318, VGAM2319, VGAM2320, VGAM2321, VGAM2322 and VGAM2323. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3219 (VGR3219) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5197] VGR3219 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3219 gene was detected is described hereinabove with reference to Figs. 1-9.

[5198] VGR3219 gene encodes VGR3219 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5199] VGR3219 precursor RNA folds spatially, forming VGR3219

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3219 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3219 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5200] VGR3219 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2324 precursor RNA, VGAM2325 precursor RNA, VGAM2326 precursor RNA, VGAM2327 precursor RNA and VGAM2328 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5201] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2324

RNA, VGAM2325 RNA, VGAM2326 RNA, VGAM2327 RNA and VGAM2328 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5202] VGAM2324 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2324 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2324 host target RNA into VGAM2324 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5203] VGAM2325 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2325 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2325 host target RNA into VGAM2325 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5204] VGAM2326 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2326 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2326 host target RNA into VGAM2326 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5205] VGAM2327 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2327 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2327 host target RNA into VGAM2327 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5206] VGAM2328 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2328 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2328 host target RNA into VGAM2328 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5207] It is appreciated that a function of VGR3219 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3219 gene include diagnosis, prevention and treatment of viral infection by

Rana Tigrina Ranavirus. Specific functions, and accordingly utilities, of VGR3219 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3219 gene: VGAM2324 host target protein, VGAM2325 host target protein, VGAM2326 host target protein, VGAM2327 host target protein and VGAM2328 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2324, VGAM2325, VGAM2326, VGAM2327 and VGAM2328. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3220(VGR3220) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5208] VGR3220 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3220 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5209] VGR3220 gene encodes VGR3220 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5210] VGR3220 precursor RNA folds spatially, forming VGR3220 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3220 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3220 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5211] VGR3220 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2329 precursor RNA, VGAM2330 precursor RNA, VGAM2331 precursor RNA, VGAM2332 precursor RNA, VGAM2333 precursor RNA, VGAM2334 precursor RNA, VGAM2335 precursor RNA and VGAM2336 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5212] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2329 RNA, VGAM2330 RNA, VGAM2331 RNA, VGAM2332 RNA, VGAM2333 RNA, VGAM2334 RNA, VGAM2335 RNA and VGAM2336 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5213] VGAM2329 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2329 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2329 host target RNA into VGAM2329 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5214] VGAM2330 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2330 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2330 host target RNA into VGAM2330 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5215] VGAM2331 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2331 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2331 host target RNA into VGAM2331 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5216] VGAM2332 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2332 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2332 host target RNA into VGAM2332 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5217] VGAM2333 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2333 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2333 host target RNA into

VGAM2333 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5218] VGAM2334 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2334 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2334 host target RNA into VGAM2334 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5219] VGAM2335 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2335 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2335 host target RNA into VGAM2335 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5220] VGAM2336 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2336 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2336 host target RNA into VGAM2336 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5221] It is appreciated that a function of VGR3220 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3220 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3220 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3220 gene: VGAM2329 host target protein, VGAM2330 host target protein, VGAM2331 host target protein, VGAM2332 host target protein, VGAM2333 host target protein, VGAM2334 host target protein, VGAM2335 host target protein and VGAM2336 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2329, VGAM2330, VGAM2331, VGAM2332, VGAM2333, VGAM2334, VGAM2335 and VGAM2336. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3221(VGR3221) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5222] VGR3221 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3221 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5223] VGR3221 gene encodes VGR3221 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5224] VGR3221 precursor RNA folds spatially, forming VGR3221 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3221 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3221 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5225] VGR3221 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2337 precursor RNA, VGAM2338 precursor RNA, VGAM2339 precursor RNA, VGAM2340 precursor RNA, VGAM2341 precursor RNA, VGAM2342 precursor RNA, VGAM2343 precursor RNA and VGAM2344 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5226] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2337 RNA, VGAM2338 RNA, VGAM2339 RNA, VGAM2340 RNA, VGAM2341 RNA, VGAM2342 RNA, VGAM2343 RNA and VGAM2344 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5227] VGAM2337 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2337 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2337 host target RNA into VGAM2337 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5228] VGAM2338 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2338 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2338 host target RNA into VGAM2338 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5229] VGAM2339 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2339 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2339 host target RNA into VGAM2339 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5230] VGAM2340 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2340 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2340 host target RNA into VGAM2340 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5231] VGAM2341 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2341 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2341 host target RNA into

VGAM2341 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5232] VGAM2342 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2342 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2342 host target RNA into VGAM2342 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5233] VGAM2343 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2343 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2343 host target RNA into VGAM2343 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5234] VGAM2344 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2344 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2344 host target RNA into VGAM2344 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5235] It is appreciated that a function of VGR3221 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3221 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3221 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3221 gene: VGAM2337 host target protein, VGAM2338 host target protein, VGAM2339 host target protein, VGAM2340 host target protein, VGAM2341 host target protein, VGAM2342 host target protein, VGAM2343 host target protein and VGAM2344 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2337, VGAM2338, VGAM2339, VGAM2340, VGAM2341, VGAM2342, VGAM2343 and VGAM2344. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3222(VGR3222) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5236] VGR3222 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3222 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5237] VGR3222 gene encodes VGR3222 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5238] VGR3222 precursor RNA folds spatially, forming VGR3222 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3222 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3222 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5239] VGR3222 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2345 precursor RNA, VGAM2346 precursor RNA, VGAM2347 precursor RNA, VGAM2348 precursor RNA, VGAM2349 precursor RNA, VGAM2350 precursor RNA, VGAM2351 precursor RNA and VGAM2352 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5240] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2345 RNA, VGAM2346 RNA, VGAM2347 RNA, VGAM2348 RNA, VGAM2349 RNA, VGAM2350 RNA, VGAM2351 RNA and VGAM2352 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5241] VGAM2345 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2345 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2345 host target RNA into VGAM2345 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5242] VGAM2346 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2346 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2346 host target RNA into VGAM2346 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5243] VGAM2347 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2347 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2347 host target RNA into VGAM2347 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5244] VGAM2348 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2348 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2348 host target RNA into VGAM2348 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5245] VGAM2349 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2349 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2349 host target RNA into

VGAM2349 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5246] VGAM2350 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2350 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2350 host target RNA into VGAM2350 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5247] VGAM2351 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2351 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2351 host target RNA into VGAM2351 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5248] VGAM2352 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2352 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2352 host target RNA into VGAM2352 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5249] It is appreciated that a function of VGR3222 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3222 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3222 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3222 gene: VGAM2345 host target protein, VGAM2346 host target protein, VGAM2347 host target protein, VGAM2348 host target protein, VGAM2349 host target protein, VGAM2350 host target protein, VGAM2351 host target protein and VGAM2352 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2345, VGAM2346, VGAM2347, VGAM2348, VGAM2349, VGAM2350, VGAM2351 and VGAM2352. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3223(VGR3223) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5250] VGR3223 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3223 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5251] VGR3223 gene encodes VGR3223 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5252] VGR3223 precursor RNA folds spatially, forming VGR3223 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3223 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3223 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5253] VGR3223 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2353 precursor RNA, VGAM2354 precursor RNA, VGAM2355 precursor RNA, VGAM2356 precursor RNA, VGAM2357 precursor RNA, VGAM2358 precursor RNA, VGAM2359 precursor RNA and VGAM2360 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5254] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2353 RNA, VGAM2354 RNA, VGAM2355 RNA, VGAM2356 RNA, VGAM2357 RNA, VGAM2358 RNA, VGAM2359 RNA and VGAM2360 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5255] VGAM2353 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2353 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2353 host target RNA into VGAM2353 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5256] VGAM2354 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2354 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2354 host target RNA into VGAM2354 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5257] VGAM2355 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2355 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2355 host target RNA into VGAM2355 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5258] VGAM2356 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2356 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2356 host target RNA into VGAM2356 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5259] VGAM2357 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2357 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2357 host target RNA into

VGAM2357 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5260] VGAM2358 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2358 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2358 host target RNA into VGAM2358 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5261] VGAM2359 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2359 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2359 host target RNA into VGAM2359 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5262] VGAM2360 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2360 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2360 host target RNA into VGAM2360 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5263] It is appreciated that a function of VGR3223 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3223 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3223 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3223 gene: VGAM2353 host target protein, VGAM2354 host target protein, VGAM2355 host target protein, VGAM2356 host target protein, VGAM2357 host target protein, VGAM2358 host target protein, VGAM2359 host target protein and VGAM2360 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2353, VGAM2354, VGAM2355, VGAM2356, VGAM2357, VGAM2358, VGAM2359 and VGAM2360. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3224(VGR3224) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5264] VGR3224 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3224 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5265] VGR3224 gene encodes VGR3224 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5266] VGR3224 precursor RNA folds spatially, forming VGR3224 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3224 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3224 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5267] VGR3224 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2361 precursor RNA, VGAM2362 precursor RNA, VGAM2363 precursor RNA and VGAM2364 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5268] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2361 RNA, VGAM2362 RNA, VGAM2363 RNA and VGAM2364 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5269] VGAM2361 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2361 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2361 host target RNA into VGAM2361 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5270] VGAM2362 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2362 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2362 host target RNA into VGAM2362 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5271] VGAM2363 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2363 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2363 host target RNA into VGAM2363 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5272] VGAM2364 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2364 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2364 host target RNA into VGAM2364 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5273] It is appreciated that a function of VGR3224 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3224 gene include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 2. Specific functions, and accordingly utilities, of VGR3224 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3224 gene: VGAM2361 host target protein, VGAM2362 host target protein, VGAM2363 host target protein and VGAM2364 host target protein,

herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein—above with reference to VGAM2361, VGAM2362, VGAM2363 and VGAM2364. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3225(VGR3225) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5274] VGR3225 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3225 gene was detected is described hereinabove with reference to Figs. 1–9.

[5275] VGR3225 gene encodes VGR3225 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5276] VGR3225 precursor RNA folds spatially, forming VGR3225 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3225 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3225 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5277] VGR3225 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2365 precursor RNA, VGAM2366 precursor RNA, VGAM2367 precursor RNA, VGAM2368 precursor RNA, VGAM2369 precursor RNA, VGAM2370 precursor RNA, VGAM2371 precursor RNA and VGAM2372 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5278] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2365 RNA, VGAM2366 RNA, VGAM2367 RNA, VGAM2368 RNA,

VGAM2369 RNA, VGAM2370 RNA, VGAM2371 RNA and VGAM2372 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5279] VGAM2365 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2365 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2365 host target RNA into VGAM2365 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5280] VGAM2366 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2366 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2366 host target RNA into VGAM2366 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5281] VGAM2367 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2367 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2367 host target RNA into VGAM2367 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5282] VGAM2368 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2368 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2368 host target RNA into VGAM2368 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5283] VGAM2369 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2369 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2369 host target RNA into VGAM2369 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5284] VGAM2370 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2370 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2370 host target RNA into VGAM2370 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5285] VGAM2371 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2371 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2371 host target RNA into VGAM2371 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5286] VGAM2372 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2372 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2372 host target RNA into VGAM2372 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5287] It is appreciated that a function of VGR3225 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3225 gene include diagnosis, prevention and treatment of viral infection by Rat Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3225 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3225 gene: VGAM2365 host target protein, VGAM2366 host target protein, VGAM2367 host target protein, VGAM2368 host target protein, VGAM2369 host target protein, VGAM2370 host target protein, VGAM2371 host target protein and VGAM2372 host target protein, herein schematically represented by

VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2365, VGAM2366, VGAM2367, VGAM2368, VGAM2369, VGAM2370, VGAM2371 and VGAM2372. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3226(VGR3226) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5288] VGR3226 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3226 gene was detected is described hereinabove with reference to Figs. 1-9.

[5289] VGR3226 gene encodes VGR3226 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5290] VGR3226 precursor RNA folds spatially, forming VGR3226 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3226 folded

precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3226 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5291] VGR3226 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2373 precursor RNA, VGAM2374 precursor RNA, VGAM2375 precursor RNA, VGAM2376 precursor RNA, VGAM2377 precursor RNA, VGAM2378 precursor RNA and VGAM2379 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5292] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2373 RNA, VGAM2374 RNA, VGAM2375 RNA, VGAM2376 RNA,

VGAM2377 RNA, VGAM2378 RNA and VGAM2379 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5293] VGAM2373 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2373 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2373 host target RNA into VGAM2373 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5294] VGAM2374 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2374 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2374 host target RNA into VGAM2374 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5295] VGAM2375 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2375 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2375 host target RNA into VGAM2375 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5296] VGAM2376 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2376 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2376 host target RNA into VGAM2376 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5297] VGAM2377 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2377 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2377 host target RNA into VGAM2377 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5298] VGAM2378 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2378 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2378 host target RNA into VGAM2378 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5299] VGAM2379 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2379 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2379 host target RNA into VGAM2379 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5300] It is appreciated that a function of VGR3226 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3226 gene include

diagnosis, prevention and treatment of viral infection by Rat Cytomegalovirus. Specific functions, and accordingly utilities, of VGR3226 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3226 gene: VGAM2373 host target protein, VGAM2374 host target protein, VGAM2375 host target protein, VGAM2376 host target protein, VGAM2377 host target protein, VGAM2378 host target protein and VGAM2379 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2373, VGAM2374, VGAM2375, VGAM2376, VGAM2377, VGAM2378 and VGAM2379. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3227(VGR3227) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5301] VGR3227 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3227 gene was detected is described hereinabove with reference to Figs. 1-9.

[5302] VGR3227 gene encodes VGR3227 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5303] VGR3227 precursor RNA folds spatially, forming VGR3227 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3227 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3227 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5304] VGR3227 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2380 precursor RNA, VGAM2381 precursor RNA, VGAM2382 precursor RNA, VGAM2383

precursor RNA, VGAM2384 precursor RNA, VGAM2385 precursor RNA and VGAM2386 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5305] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2380 RNA, VGAM2381 RNA, VGAM2382 RNA, VGAM2383 RNA, VGAM2384 RNA, VGAM2385 RNA and VGAM2386 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5306] VGAM2380 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2380 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2380 host target RNA into VGAM2380 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5307] VGAM2381 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2381 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2381 host target RNA into VGAM2381 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5308] VGAM2382 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2382 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2382 host target RNA into VGAM2382 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5309] VGAM2383 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2383 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2383 host target RNA into VGAM2383 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5310] VGAM2384 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2384 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2384 host target RNA into VGAM2384 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5311] VGAM2385 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2385 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2385 host target RNA into VGAM2385 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5312] VGAM2386 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2386 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2386 host target RNA into VGAM2386 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5313] It is appreciated that a function of VGR3227 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3227 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3227 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3227 gene: VGAM2380 host target protein, VGAM2381 host target protein, VGAM2382 host target protein, VGAM2383 host target protein, VGAM2384 host target protein, VGAM2385 host target protein and VGAM2386 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM2380, VGAM2381, VGAM2382, VGAM2383, VGAM2384, VGAM2385 and VGAM2386. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3228(VGR3228) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5314] VGR3228 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3228 gene was detected is described hereinabove with reference to Figs. 1-9.

[5315] VGR3228 gene encodes VGR3228 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5316] VGR3228 precursor RNA folds spatially, forming VGR3228 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3228 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3228 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5317] VGR3228 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2387 precursor RNA and VGAM2388 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5318] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2387 RNA and VGAM2388 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5319] VGAM2387 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2387 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2387 host target RNA into VGAM2387 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5320] VGAM2388 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2388 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2388 host target RNA into VGAM2388 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5321] It is appreciated that a function of VGR3228 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3228 gene include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 4. Specific functions, and accordingly utilities, of VGR3228 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3228 gene: VGAM2387 host target protein and VGAM2388 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2387 and VGAM2388. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3229(VGR3229) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5322] VGR3229 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3229 gene was detected is described hereinabove with reference to Figs. 1-9.

[5323] VGR3229 gene encodes VGR3229 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5324] VGR3229 precursor RNA folds spatially, forming VGR3229 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3229 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3229 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5325] VGR3229 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2389 precursor RNA, VGAM2390 precursor RNA, VGAM2391 precursor RNA, VGAM2392 precursor RNA, VGAM2393 precursor RNA, VGAM2394

precursor RNA, VGAM2395 precursor RNA and VGAM2396 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5326] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2389 RNA, VGAM2390 RNA, VGAM2391 RNA, VGAM2392 RNA, VGAM2393 RNA, VGAM2394 RNA, VGAM2395 RNA and VGAM2396 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5327] VGAM2389 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2389 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2389 host target RNA into

VGAM2389 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5328] VGAM2390 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2390 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2390 host target RNA into VGAM2390 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5329] VGAM2391 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2391 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2391 host target RNA into VGAM2391 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5330] VGAM2392 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2392 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2392 host target RNA into VGAM2392 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5331] VGAM2393 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2393 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2393 host target RNA into VGAM2393 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5332] VGAM2394 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2394 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2394 host target RNA into VGAM2394 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5333] VGAM2395 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2395 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2395 host target RNA into VGAM2395 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5334] VGAM2396 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2396 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2396 host target RNA into VGAM2396 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5335] It is appreciated that a function of VGR3229 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3229 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3229 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3229 gene: VGAM2389 host target protein, VGAM2390 host target protein, VGAM2391 host target protein, VGAM2392 host target protein, VGAM2393 host target protein, VGAM2394 host target protein, VGAM2395 host target protein and VGAM2396 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2389, VGAM2390, VGAM2391, VGAM2392, VGAM2393, VGAM2394, VGAM2395 and VGAM2396. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3230(VGR3230) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5336] VGR3230 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3230 gene was detected is described hereinabove with reference to Figs. 1-9.

[5337] VGR3230 gene encodes VGR3230 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5338] VGR3230 precursor RNA folds spatially, forming VGR3230 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3230 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3230 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5339] VGR3230 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2397 precursor RNA, VGAM2398 precursor RNA, VGAM2399 precursor RNA, VGAM2400 precursor RNA, VGAM2401 precursor RNA, VGAM2402

precursor RNA, VGAM2403 precursor RNA and VGAM2404 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5340] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2397 RNA, VGAM2398 RNA, VGAM2399 RNA, VGAM2400 RNA, VGAM2401 RNA, VGAM2402 RNA, VGAM2403 RNA and VGAM2404 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5341] VGAM2397 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2397 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2397 host target RNA into

VGAM2397 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5342] VGAM2398 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2398 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2398 host target RNA into VGAM2398 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5343] VGAM2399 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2399 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2399 host target RNA into VGAM2399 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5344] VGAM2400 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2400 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2400 host target RNA into VGAM2400 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5345] VGAM2401 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2401 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2401 host target RNA into VGAM2401 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5346] VGAM2402 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2402 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2402 host target RNA into VGAM2402 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5347] VGAM2403 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2403 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2403 host target RNA into VGAM2403 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5348] VGAM2404 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2404 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2404 host target RNA into VGAM2404 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5349] It is appreciated that a function of VGR3230 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3230 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3230 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3230 gene: VGAM2397 host target protein, VGAM2398 host target protein, VGAM2399 host target protein, VGAM2400 host target protein, VGAM2401 host target protein, VGAM2402 host target protein, VGAM2403 host target protein and VGAM2404 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2397, VGAM2398, VGAM2399, VGAM2400, VGAM2401, VGAM2402, VGAM2403 and VGAM2404. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3231(VGR3231) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5350] VGR3231 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3231 gene was detected is described hereinabove with reference to Figs. 1-9.

[5351] VGR3231 gene encodes VGR3231 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5352] VGR3231 precursor RNA folds spatially, forming VGR3231 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3231 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3231 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5353] VGR3231 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2405 precursor RNA, VGAM2406 precursor RNA, VGAM2407 precursor RNA, VGAM2408 precursor RNA, VGAM2409 precursor RNA, VGAM2410

precursor RNA, VGAM2411 precursor RNA and VGAM2412 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5354] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2405 RNA, VGAM2406 RNA, VGAM2407 RNA, VGAM2408 RNA, VGAM2409 RNA, VGAM2410 RNA, VGAM2411 RNA and VGAM2412 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5355] VGAM2405 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2405 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2405 host target RNA into

VGAM2405 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5356] VGAM2406 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2406 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2406 host target RNA into VGAM2406 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5357] VGAM2407 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2407 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2407 host target RNA into VGAM2407 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5358] VGAM2408 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2408 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2408 host target RNA into VGAM2408 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5359] VGAM2409 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2409 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2409 host target RNA into VGAM2409 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5360] VGAM2410 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2410 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2410 host target RNA into VGAM2410 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5361] VGAM2411 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2411 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2411 host target RNA into VGAM2411 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5362] VGAM2412 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2412 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2412 host target RNA into VGAM2412 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5363] It is appreciated that a function of VGR3231 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3231 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3231 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3231 gene: VGAM2405 host target protein, VGAM2406 host target protein, VGAM2407 host target protein, VGAM2408 host target protein, VGAM2409 host target protein, VGAM2410 host target protein, VGAM2411 host target protein and VGAM2412 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2405, VGAM2406, VGAM2407, VGAM2408, VGAM2409, VGAM2410, VGAM2411 and VGAM2412. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3232(VGR3232) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5364] VGR3232 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3232 gene was detected is described hereinabove with reference to Figs. 1-9.

[5365] VGR3232 gene encodes VGR3232 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5366] VGR3232 precursor RNA folds spatially, forming VGR3232 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3232 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3232 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5367] VGR3232 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2413 precursor RNA, VGAM2414 precursor RNA, VGAM2415 precursor RNA, VGAM2416 precursor RNA, VGAM2417 precursor RNA, VGAM2418

precursor RNA, VGAM2419 precursor RNA and VGAM2420 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5368] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2413 RNA, VGAM2414 RNA, VGAM2415 RNA, VGAM2416 RNA, VGAM2417 RNA, VGAM2418 RNA, VGAM2419 RNA and VGAM2420 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5369] VGAM2413 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2413 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2413 host target RNA into

VGAM2413 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5370] VGAM2414 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2414 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2414 host target RNA into VGAM2414 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5371] VGAM2415 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2415 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2415 host target RNA into VGAM2415 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5372] VGAM2416 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2416 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2416 host target RNA into VGAM2416 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5373] VGAM2417 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2417 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2417 host target RNA into VGAM2417 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5374] VGAM2418 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2418 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2418 host target RNA into VGAM2418 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5375] VGAM2419 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2419 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2419 host target RNA into VGAM2419 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5376] VGAM2420 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2420 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2420 host target RNA into VGAM2420 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5377] It is appreciated that a function of VGR3232 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3232 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3232 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3232 gene: VGAM2413 host target protein, VGAM2414 host target protein, VGAM2415 host target protein, VGAM2416 host target protein, VGAM2417 host target protein, VGAM2418 host target protein, VGAM2419 host target protein and VGAM2420 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2413, VGAM2414, VGAM2415, VGAM2416, VGAM2417, VGAM2418, VGAM2419 and VGAM2420. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3233(VGR3233) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5378] VGR3233 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3233 gene was detected is described hereinabove with reference to Figs. 1-9.

[5379] VGR3233 gene encodes VGR3233 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5380] VGR3233 precursor RNA folds spatially, forming VGR3233 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3233 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3233 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5381] VGR3233 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2421 precursor RNA, VGAM2422 precursor RNA, VGAM2423 precursor RNA, VGAM2424 precursor RNA, VGAM2425 precursor RNA, VGAM2426

precursor RNA, VGAM2427 precursor RNA and VGAM2428 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5382] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2421 RNA, VGAM2422 RNA, VGAM2423 RNA, VGAM2424 RNA, VGAM2425 RNA, VGAM2426 RNA, VGAM2427 RNA and VGAM2428 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5383] VGAM2421 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2421 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2421 host target RNA into

VGAM2421 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5384] VGAM2422 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2422 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2422 host target RNA into VGAM2422 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5385] VGAM2423 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2423 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2423 host target RNA into VGAM2423 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5386] VGAM2424 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2424 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2424 host target RNA into VGAM2424 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5387] VGAM2425 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2425 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2425 host target RNA into VGAM2425 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5388] VGAM2426 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2426 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2426 host target RNA into VGAM2426 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5389] VGAM2427 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2427 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2427 host target RNA into VGAM2427 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5390] VGAM2428 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2428 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2428 host target RNA into VGAM2428 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5391] It is appreciated that a function of VGR3233 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3233 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3233 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3233 gene: VGAM2421 host target protein, VGAM2422 host target protein, VGAM2423 host target protein, VGAM2424 host target protein, VGAM2425 host target protein, VGAM2426 host target protein, VGAM2427 host target protein and VGAM2428 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2421, VGAM2422, VGAM2423, VGAM2424, VGAM2425, VGAM2426, VGAM2427 and VGAM2428. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3234(VGR3234) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5392] VGR3234 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3234 gene was detected is described hereinabove with reference to Figs. 1-9.

[5393] VGR3234 gene encodes VGR3234 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5394] VGR3234 precursor RNA folds spatially, forming VGR3234 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3234 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3234 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5395] VGR3234 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2429 precursor RNA, VGAM2430 precursor RNA, VGAM2431 precursor RNA, VGAM2432 precursor RNA, VGAM2433 precursor RNA, VGAM2434

precursor RNA, VGAM2435 precursor RNA and VGAM2436 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5396] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2429 RNA, VGAM2430 RNA, VGAM2431 RNA, VGAM2432 RNA, VGAM2433 RNA, VGAM2434 RNA, VGAM2435 RNA and VGAM2436 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5397] VGAM2429 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2429 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2429 host target RNA into

VGAM2429 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5398] VGAM2430 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2430 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2430 host target RNA into VGAM2430 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5399] VGAM2431 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2431 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2431 host target RNA into VGAM2431 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5400] VGAM2432 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2432 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2432 host target RNA into VGAM2432 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5401] VGAM2433 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2433 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2433 host target RNA into VGAM2433 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5402] VGAM2434 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2434 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2434 host target RNA into VGAM2434 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5403] VGAM2435 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2435 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2435 host target RNA into VGAM2435 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5404] VGAM2436 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2436 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2436 host target RNA into VGAM2436 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5405] It is appreciated that a function of VGR3234 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3234 gene include diagnosis, prevention and treatment of viral infection by

Goatpox Virus. Specific functions, and accordingly utilities, of VGR3234 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3234 gene: VGAM2429 host target protein, VGAM2430 host target protein, VGAM2431 host target protein, VGAM2432 host target protein, VGAM2433 host target protein, VGAM2434 host target protein, VGAM2435 host target protein and VGAM2436 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2429, VGAM2430, VGAM2431, VGAM2432, VGAM2433, VGAM2434, VGAM2435 and VGAM2436. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3235 (VGR3235) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5406] VGR3235 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3235 gene was detected is described hereinabove with reference to Figs. 1-9.

[5407] VGR3235 gene encodes VGR3235 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5408] VGR3235 precursor RNA folds spatially, forming VGR3235 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3235 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3235 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5409] VGR3235 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2437 precursor RNA, VGAM2438 precursor RNA, VGAM2439 precursor RNA, VGAM2440 precursor RNA, VGAM2441 precursor RNA and VGAM2442

precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5410] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2437 RNA, VGAM2438 RNA, VGAM2439 RNA, VGAM2440 RNA, VGAM2441 RNA and VGAM2442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5411] VGAM2437 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2437 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2437 host target RNA into VGAM2437 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5412] VGAM2438 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2438 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2438 host target RNA into VGAM2438 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5413] VGAM2439 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2439 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2439 host target RNA into

VGAM2439 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5414] VGAM2440 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2440 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2440 host target RNA into VGAM2440 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5415] VGAM2441 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2441 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2441 host target RNA into VGAM2441 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5416] VGAM2442 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2442 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2442 host target RNA into VGAM2442 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5417] It is appreciated that a function of VGR3235 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3235 gene include diagnosis, prevention and treatment of viral infection by Goatpox Virus. Specific functions, and accordingly utilities, of VGR3235 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3235 gene: VGAM2437 host target protein, VGAM2438 host target protein, VGAM2439 host target protein, VGAM2440 host target protein, VGAM2441 host target protein and VGAM2442 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2437, VGAM2438, VGAM2439, VGAM2440, VGAM2441 and VGAM2442. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3236(VGR3236) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5418] VGR3236 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3236 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5419] VGR3236 gene encodes VGR3236 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5420] VGR3236 precursor RNA folds spatially, forming VGR3236 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3236 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3236 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5421] VGR3236 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2443 precursor RNA, VGAM2444 precursor RNA, VGAM2445 precursor RNA, VGAM2446 precursor RNA, VGAM2447 precursor RNA, VGAM2448 precursor RNA, VGAM2449 precursor RNA and VGAM2450 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5422] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2443 RNA, VGAM2444 RNA, VGAM2445 RNA, VGAM2446 RNA, VGAM2447 RNA, VGAM2448 RNA, VGAM2449 RNA and VGAM2450 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5423] VGAM2443 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2443 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2443 host target RNA into VGAM2443 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5424] VGAM2444 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2444 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2444 host target RNA into VGAM2444 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5425] VGAM2445 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2445 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2445 host target RNA into VGAM2445 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5426] VGAM2446 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2446 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2446 host target RNA into VGAM2446 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5427] VGAM2447 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2447 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2447 host target RNA into VGAM2447 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5428] VGAM2448 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2448 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2448 host target RNA into VGAM2448 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5429] VGAM2449 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2449 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2449 host target RNA into

VGAM2449 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5430] VGAM2450 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2450 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2450 host target RNA into VGAM2450 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5431] It is appreciated that a function of VGR3236 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3236 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3236 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3236 gene: VGAM2443 host
target protein, VGAM2444 host target protein, VGAM2445
host target protein, VGAM2446 host target protein,
VGAM2447 host target protein, VGAM2448 host target
protein, VGAM2449 host target protein and VGAM2450
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2443,
VGAM2444, VGAM2445, VGAM2446, VGAM2447,
VGAM2448, VGAM2449 and VGAM2450. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3237(VGR3237) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5432] VGR3237 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3237 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [5433] VGR3237 gene encodes VGR3237 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5434] VGR3237 precursor RNA folds spatially, forming VGR3237 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3237 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3237 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5435] VGR3237 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2451 precursor RNA, VGAM2452 precursor RNA, VGAM2453 precursor RNA, VGAM2454 precursor RNA, VGAM2455 precursor RNA, VGAM2456 precursor RNA, VGAM2457 precursor RNA and VGAM2458 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5436] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2451 RNA, VGAM2452 RNA, VGAM2453 RNA, VGAM2454 RNA, VGAM2455 RNA, VGAM2456 RNA, VGAM2457 RNA and VGAM2458 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5437] VGAM2451 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2451 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2451 host target RNA into VGAM2451 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5438] VGAM2452 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2452 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2452 host target RNA into VGAM2452 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5439] VGAM2453 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2453 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2453 host target RNA into VGAM2453 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5440] VGAM2454 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2454 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2454 host target RNA into VGAM2454 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5441] VGAM2455 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2455 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2455 host target RNA into VGAM2455 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5442] VGAM2456 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2456 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2456 host target RNA into VGAM2456 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5443] VGAM2457 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2457 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2457 host target RNA into

VGAM2457 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5444] VGAM2458 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2458 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2458 host target RNA into VGAM2458 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5445] It is appreciated that a function of VGR3237 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3237 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3237 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3237 gene: VGAM2451 host
target protein, VGAM2452 host target protein, VGAM2453
host target protein, VGAM2454 host target protein,
VGAM2455 host target protein, VGAM2456 host target
protein, VGAM2457 host target protein and VGAM2458
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2451,
VGAM2452, VGAM2453, VGAM2454, VGAM2455,
VGAM2456, VGAM2457 and VGAM2458. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3238(VGR3238) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5446] VGR3238 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3238 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [5447] VGR3238 gene encodes VGR3238 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5448] VGR3238 precursor RNA folds spatially, forming VGR3238 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3238 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3238 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5449] VGR3238 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2459 precursor RNA, VGAM2460 precursor RNA, VGAM2461 precursor RNA, VGAM2462 precursor RNA, VGAM2463 precursor RNA, VGAM2464 precursor RNA, VGAM2465 precursor RNA and VGAM2466 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5450] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2459 RNA, VGAM2460 RNA, VGAM2461 RNA, VGAM2462 RNA, VGAM2463 RNA, VGAM2464 RNA, VGAM2465 RNA and VGAM2466 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5451] VGAM2459 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2459 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2459 host target RNA into VGAM2459 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5452] VGAM2460 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2460 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2460 host target RNA into VGAM2460 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5453] VGAM2461 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2461 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2461 host target RNA into VGAM2461 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5454] VGAM2462 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2462 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2462 host target RNA into VGAM2462 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5455] VGAM2463 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2463 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2463 host target RNA into VGAM2463 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5456] VGAM2464 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2464 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2464 host target RNA into VGAM2464 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5457] VGAM2465 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2465 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2465 host target RNA into

VGAM2465 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5458] VGAM2466 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2466 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2466 host target RNA into VGAM2466 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5459] It is appreciated that a function of VGR3238 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3238 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3238 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3238 gene: VGAM2459 host target protein, VGAM2460 host target protein, VGAM2461 host target protein, VGAM2462 host target protein, VGAM2463 host target protein, VGAM2464 host target protein, VGAM2465 host target protein and VGAM2466 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2459, VGAM2460, VGAM2461, VGAM2462, VGAM2463, VGAM2464, VGAM2465 and VGAM2466. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3239(VGR3239) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5460] VGR3239 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3239 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5461] VGR3239 gene encodes VGR3239 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5462] VGR3239 precursor RNA folds spatially, forming VGR3239 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3239 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3239 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5463] VGR3239 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2467 precursor RNA, VGAM2468 precursor RNA, VGAM2469 precursor RNA, VGAM2470 precursor RNA, VGAM2471 precursor RNA, VGAM2472 precursor RNA, VGAM2473 precursor RNA and VGAM2474 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5464] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2467 RNA, VGAM2468 RNA, VGAM2469 RNA, VGAM2470 RNA, VGAM2471 RNA, VGAM2472 RNA, VGAM2473 RNA and VGAM2474 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5465] VGAM2467 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2467 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2467 host target RNA into VGAM2467 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5466] VGAM2468 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2468 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2468 host target RNA into VGAM2468 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5467] VGAM2469 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2469 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2469 host target RNA into VGAM2469 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5468] VGAM2470 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2470 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2470 host target RNA into VGAM2470 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5469] VGAM2471 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2471 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2471 host target RNA into VGAM2471 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5470] VGAM2472 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2472 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2472 host target RNA into VGAM2472 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5471] VGAM2473 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2473 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2473 host target RNA into

VGAM2473 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5472] VGAM2474 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2474 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2474 host target RNA into VGAM2474 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5473] It is appreciated that a function of VGR3239 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3239 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3239 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3239 gene: VGAM2467 host
target protein, VGAM2468 host target protein, VGAM2469
host target protein, VGAM2470 host target protein,
VGAM2471 host target protein, VGAM2472 host target
protein, VGAM2473 host target protein and VGAM2474
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2467,
VGAM2468, VGAM2469, VGAM2470, VGAM2471,
VGAM2472, VGAM2473 and VGAM2474. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3240(VGR3240) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5474] VGR3240 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3240 gene was
detected is described hereinabove with reference to Figs.

1-9.

- [5475] VGR3240 gene encodes VGR3240 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5476] VGR3240 precursor RNA folds spatially, forming VGR3240 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3240 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3240 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5477] VGR3240 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2475 precursor RNA, VGAM2476 precursor RNA, VGAM2477 precursor RNA, VGAM2478 precursor RNA, VGAM2479 precursor RNA, VGAM2480 precursor RNA, VGAM2481 precursor RNA and VGAM2482 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5478] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2475 RNA, VGAM2476 RNA, VGAM2477 RNA, VGAM2478 RNA, VGAM2479 RNA, VGAM2480 RNA, VGAM2481 RNA and VGAM2482 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5479] VGAM2475 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2475 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2475 host target RNA into VGAM2475 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5480] VGAM2476 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2476 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2476 host target RNA into VGAM2476 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5481] VGAM2477 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2477 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2477 host target RNA into VGAM2477 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5482] VGAM2478 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2478 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2478 host target RNA into VGAM2478 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5483] VGAM2479 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2479 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2479 host target RNA into VGAM2479 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5484] VGAM2480 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2480 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2480 host target RNA into VGAM2480 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5485] VGAM2481 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2481 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2481 host target RNA into

VGAM2481 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5486] VGAM2482 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2482 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2482 host target RNA into VGAM2482 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5487] It is appreciated that a function of VGR3240 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3240 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3240 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3240 gene: VGAM2475 host target protein, VGAM2476 host target protein, VGAM2477 host target protein, VGAM2478 host target protein, VGAM2479 host target protein, VGAM2480 host target protein, VGAM2481 host target protein and VGAM2482 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2475, VGAM2476, VGAM2477, VGAM2478, VGAM2479, VGAM2480, VGAM2481 and VGAM2482. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3241(VGR3241) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5488] VGR3241 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3241 gene was detected is described hereinabove with reference to Figs.

1-9.

[5489] VGR3241 gene encodes VGR3241 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5490] VGR3241 precursor RNA folds spatially, forming VGR3241 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3241 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3241 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5491] VGR3241 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2483 precursor RNA, VGAM2484 precursor RNA, VGAM2485 precursor RNA, VGAM2486 precursor RNA, VGAM2487 precursor RNA, VGAM2488 precursor RNA, VGAM2489 precursor RNA and VGAM2490 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5492] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2483 RNA, VGAM2484 RNA, VGAM2485 RNA, VGAM2486 RNA, VGAM2487 RNA, VGAM2488 RNA, VGAM2489 RNA and VGAM2490 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5493] VGAM2483 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2483 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2483 host target RNA into VGAM2483 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5494] VGAM2484 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2484 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2484 host target RNA into VGAM2484 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5495] VGAM2485 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2485 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2485 host target RNA into VGAM2485 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5496] VGAM2486 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2486 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2486 host target RNA into VGAM2486 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5497] VGAM2487 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2487 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2487 host target RNA into VGAM2487 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5498] VGAM2488 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2488 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2488 host target RNA into VGAM2488 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5499] VGAM2489 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2489 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2489 host target RNA into

VGAM2489 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5500] VGAM2490 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2490 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2490 host target RNA into VGAM2490 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5501] It is appreciated that a function of VGR3241 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3241 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3241 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3241 gene: VGAM2483 host
target protein, VGAM2484 host target protein, VGAM2485
host target protein, VGAM2486 host target protein,
VGAM2487 host target protein, VGAM2488 host target
protein, VGAM2489 host target protein and VGAM2490
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2483,
VGAM2484, VGAM2485, VGAM2486, VGAM2487,
VGAM2488, VGAM2489 and VGAM2490. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3242(VGR3242) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5502] VGR3242 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3242 gene was
detected is described hereinabove with reference to Figs.

1-9.

[5503] VGR3242 gene encodes VGR3242 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5504] VGR3242 precursor RNA folds spatially, forming VGR3242 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3242 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3242 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5505] VGR3242 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2491 precursor RNA, VGAM2492 precursor RNA, VGAM2493 precursor RNA, VGAM2494 precursor RNA, VGAM2495 precursor RNA, VGAM2496 precursor RNA, VGAM2497 precursor RNA and VGAM2498 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5506] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2491 RNA, VGAM2492 RNA, VGAM2493 RNA, VGAM2494 RNA, VGAM2495 RNA, VGAM2496 RNA, VGAM2497 RNA and VGAM2498 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5507] VGAM2491 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2491 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2491 host target RNA into VGAM2491 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5508] VGAM2492 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2492 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2492 host target RNA into VGAM2492 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5509] VGAM2493 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2493 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2493 host target RNA into VGAM2493 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5510] VGAM2494 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2494 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2494 host target RNA into VGAM2494 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5511] VGAM2495 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2495 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2495 host target RNA into VGAM2495 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5512] VGAM2496 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2496 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2496 host target RNA into VGAM2496 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5513] VGAM2497 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2497 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2497 host target RNA into

VGAM2497 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5514] VGAM2498 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2498 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2498 host target RNA into VGAM2498 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5515] It is appreciated that a function of VGR3242 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3242 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3242 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3242 gene: VGAM2491 host target protein, VGAM2492 host target protein, VGAM2493 host target protein, VGAM2494 host target protein, VGAM2495 host target protein, VGAM2496 host target protein, VGAM2497 host target protein and VGAM2498 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2491, VGAM2492, VGAM2493, VGAM2494, VGAM2495, VGAM2496, VGAM2497 and VGAM2498. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3243(VGR3243) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5516] VGR3243 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3243 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5517] VGR3243 gene encodes VGR3243 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5518] VGR3243 precursor RNA folds spatially, forming VGR3243 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3243 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3243 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5519] VGR3243 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2499 precursor RNA, VGAM2500 precursor RNA, VGAM2501 precursor RNA, VGAM2502 precursor RNA, VGAM2503 precursor RNA, VGAM2504 precursor RNA, VGAM2505 precursor RNA and VGAM2506 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5520] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2499 RNA, VGAM2500 RNA, VGAM2501 RNA, VGAM2502 RNA, VGAM2503 RNA, VGAM2504 RNA, VGAM2505 RNA and VGAM2506 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5521] VGAM2499 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2499 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2499 host target RNA into VGAM2499 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5522] VGAM2500 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2500 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2500 host target RNA into VGAM2500 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5523] VGAM2501 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2501 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2501 host target RNA into VGAM2501 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5524] VGAM2502 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2502 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2502 host target RNA into VGAM2502 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5525] VGAM2503 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2503 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2503 host target RNA into VGAM2503 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5526] VGAM2504 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2504 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2504 host target RNA into VGAM2504 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5527] VGAM2505 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2505 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2505 host target RNA into

VGAM2505 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5528] VGAM2506 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2506 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2506 host target RNA into VGAM2506 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5529] It is appreciated that a function of VGR3243 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3243 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3243 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3243 gene: VGAM2499 host
target protein, VGAM2500 host target protein, VGAM2501
host target protein, VGAM2502 host target protein,
VGAM2503 host target protein, VGAM2504 host target
protein, VGAM2505 host target protein and VGAM2506
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2499,
VGAM2500, VGAM2501, VGAM2502, VGAM2503,
VGAM2504, VGAM2505 and VGAM2506. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3244(VGR3244) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5530] VGR3244 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3244 gene was
detected is described hereinabove with reference to Figs.

1-9.

[5531] VGR3244 gene encodes VGR3244 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5532] VGR3244 precursor RNA folds spatially, forming VGR3244 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3244 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3244 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5533] VGR3244 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2507 precursor RNA, VGAM2508 precursor RNA, VGAM2509 precursor RNA, VGAM2510 precursor RNA, VGAM2511 precursor RNA, VGAM2512 precursor RNA, VGAM2513 precursor RNA and VGAM2514 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5534] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2507 RNA, VGAM2508 RNA, VGAM2509 RNA, VGAM2510 RNA, VGAM2511 RNA, VGAM2512 RNA, VGAM2513 RNA and VGAM2514 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5535] VGAM2507 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2507 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2507 host target RNA into VGAM2507 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5536] VGAM2508 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2508 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2508 host target RNA into VGAM2508 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5537] VGAM2509 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2509 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2509 host target RNA into VGAM2509 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5538] VGAM2510 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2510 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2510 host target RNA into VGAM2510 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5539] VGAM2511 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2511 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2511 host target RNA into VGAM2511 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5540] VGAM2512 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2512 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2512 host target RNA into VGAM2512 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5541] VGAM2513 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2513 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2513 host target RNA into

VGAM2513 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5542] VGAM2514 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2514 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2514 host target RNA into VGAM2514 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5543] It is appreciated that a function of VGR3244 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3244 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3244 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3244 gene: VGAM2507 host target protein, VGAM2508 host target protein, VGAM2509 host target protein, VGAM2510 host target protein, VGAM2511 host target protein, VGAM2512 host target protein, VGAM2513 host target protein and VGAM2514 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2507, VGAM2508, VGAM2509, VGAM2510, VGAM2511, VGAM2512, VGAM2513 and VGAM2514. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3245(VGR3245) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5544] VGR3245 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3245 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5545] VGR3245 gene encodes VGR3245 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5546] VGR3245 precursor RNA folds spatially, forming VGR3245 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3245 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3245 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5547] VGR3245 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2515 precursor RNA, VGAM2516 precursor RNA, VGAM2517 precursor RNA, VGAM2518 precursor RNA, VGAM2519 precursor RNA, VGAM2520 precursor RNA, VGAM2521 precursor RNA and VGAM2522 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5548] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2515 RNA, VGAM2516 RNA, VGAM2517 RNA, VGAM2518 RNA, VGAM2519 RNA, VGAM2520 RNA, VGAM2521 RNA and VGAM2522 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5549] VGAM2515 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2515 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2515 host target RNA into VGAM2515 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5550] VGAM2516 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2516 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2516 host target RNA into VGAM2516 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5551] VGAM2517 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2517 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2517 host target RNA into VGAM2517 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5552] VGAM2518 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2518 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2518 host target RNA into VGAM2518 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5553] VGAM2519 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2519 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2519 host target RNA into VGAM2519 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5554] VGAM2520 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2520 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2520 host target RNA into VGAM2520 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5555] VGAM2521 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2521 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2521 host target RNA into

VGAM2521 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5556] VGAM2522 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2522 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2522 host target RNA into VGAM2522 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5557] It is appreciated that a function of VGR3245 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3245 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3245 gene correlate with, and may be deduced from, the identity of the host target genes,

which are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3245 gene: VGAM2515 host
target protein, VGAM2516 host target protein, VGAM2517
host target protein, VGAM2518 host target protein,
VGAM2519 host target protein, VGAM2520 host target
protein, VGAM2521 host target protein and VGAM2522
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2515,
VGAM2516, VGAM2517, VGAM2518, VGAM2519,
VGAM2520, VGAM2521 and VGAM2522. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3246(VGR3246) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5558] VGR3246 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3246 gene was
detected is described hereinabove with reference to Figs.

1-9.

[5559] VGR3246 gene encodes VGR3246 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5560] VGR3246 precursor RNA folds spatially, forming VGR3246 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3246 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3246 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5561] VGR3246 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2523 precursor RNA, VGAM2524 precursor RNA, VGAM2525 precursor RNA, VGAM2526 precursor RNA and VGAM2527 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5562] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2523 RNA, VGAM2524 RNA, VGAM2525 RNA, VGAM2526 RNA and VGAM2527 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5563] VGAM2523 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2523 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2523 host target RNA into VGAM2523 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5564] VGAM2524 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2524 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2524 host target RNA into VGAM2524 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5565] VGAM2525 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2525 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2525 host target RNA into VGAM2525 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5566] VGAM2526 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2526 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2526 host target RNA into VGAM2526 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5567] VGAM2527 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2527 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2527 host target RNA into VGAM2527 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5568] It is appreciated that a function of VGR3246 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3246 gene include diagnosis, prevention and treatment of viral infection by Mouse Cytomegalovirus 1. Specific functions, and accordingly utilities, of VGR3246 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3246 gene: VGAM2523 host target protein, VGAM2524 host target protein, VGAM2525 host target protein, VGAM2526 host target protein and VGAM2527 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2523, VGAM2524, VGAM2525, VGAM2526 and VGAM2527. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3247(VGR3247) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one

host target gene, the function and utility of which at least one host target gene is known in the art.

[5569] VGR3247 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3247 gene was detected is described hereinabove with reference to Figs. 1-9.

[5570] VGR3247 gene encodes VGR3247 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5571] VGR3247 precursor RNA folds spatially, forming VGR3247 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3247 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3247 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5572] VGR3247 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM

precursor RNAs, VGAM2530 precursor RNA and VGAM2531 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5573] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2530 RNA and VGAM2531 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5574] VGAM2530 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2530 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2530 host target RNA into VGAM2530 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5575] VGAM2531 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2531 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2531 host target RNA into VGAM2531 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5576] It is appreciated that a function of VGR3247 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3247 gene include diagnosis, prevention and treatment of viral infection by Pepper Ringspot Virus. Specific functions, and accordingly utilities, of VGR3247 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3247 gene: VGAM2530 host

target protein and VGAM2531 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2530 and VGAM2531. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3248(VGR3248) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5577] VGR3248 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3248 gene was detected is described hereinabove with reference to Figs. 1-9.

[5578] VGR3248 gene encodes VGR3248 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5579] VGR3248 precursor RNA folds spatially, forming VGR3248 folded precursor RNA, herein designated VGR FOLDED

PRECURSOR RNA. It is appreciated that VGR3248 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3248 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5580] VGR3248 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2532 precursor RNA, VGAM2533 precursor RNA, VGAM2534 precursor RNA and VGAM2535 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5581] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2532 RNA, VGAM2533 RNA, VGAM2534 RNA and VGAM2535 RNA, herein schematically represented by VGAM1 RNA

through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5582] VGAM2532 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2532 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2532 host target RNA into VGAM2532 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5583] VGAM2533 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2533 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2533 host target RNA into

VGAM2533 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5584] VGAM2534 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2534 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2534 host target RNA into VGAM2534 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5585] VGAM2535 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2535 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2535 host target RNA into VGAM2535 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5586] It is appreciated that a function of VGR3248 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3248 gene include diagnosis, prevention and treatment of viral infection by Rio Bravo Virus. Specific functions, and accordingly utilities, of VGR3248 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3248 gene: VGAM2532 host target protein, VGAM2533 host target protein, VGAM2534 host target protein and VGAM2535 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2532, VGAM2533, VGAM2534 and VGAM2535. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic

Record 3249(VGR3249) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[5587] VGR3249 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3249 gene was
detected is described hereinabove with reference to Figs.
1-9.

[5588] VGR3249 gene encodes VGR3249 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[5589] VGR3249 precursor RNA folds spatially, forming VGR3249
folded precursor RNA, herein designated VGR FOLDED
PRECURSOR RNA. It is appreciated that VGR3249 folded
precursor RNA comprises a plurality of what is known in
the art as `hairpin` structures. These `hairpin` structures
are due to the fact that the nucleotide sequence of
VGR3249 precursor RNA comprises a plurality of seg-
ments, the first half of each such segment having a nu-
cleotide sequence which is at least a partial inversed-re-
versed sequence of the second half thereof, as is well

known in the art.

[5590] VGR3249 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2536 precursor RNA, VGAM2537 precursor RNA and VGAM2538 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5591] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2536 RNA, VGAM2537 RNA and VGAM2538 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5592] VGAM2536 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2536 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2536 host target RNA into VGAM2536 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5593] VGAM2537 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2537 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2537 host target RNA into VGAM2537 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5594] VGAM2538 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2538 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2538 host target RNA into VGAM2538 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5595] It is appreciated that a function of VGR3249 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3249 gene include diagnosis, prevention and treatment of viral infection by Pestivirus Reindeer-1. Specific functions, and accordingly utilities, of VGR3249 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3249 gene: VGAM2536 host target protein, VGAM2537 host target protein and VGAM2538 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2536, VGAM2537 and VGAM2538. Fig. 9

further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3250(VGR3250) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5596] VGR3250 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3250 gene was detected is described hereinabove with reference to Figs. 1-9.

[5597] VGR3250 gene encodes VGR3250 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5598] VGR3250 precursor RNA folds spatially, forming VGR3250 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3250 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3250 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5599] VGR3250 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2539 precursor RNA and VGAM2540 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5600] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2539 RNA and VGAM2540 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5601] VGAM2539 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2539 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2539 host target RNA into VGAM2539 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5602] VGAM2540 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2540 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2540 host target RNA into VGAM2540 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5603] It is appreciated that a function of VGR3250 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3250 gene include

diagnosis, prevention and treatment of viral infection by Pestivirus Giraffe-1. Specific functions, and accordingly utilities, of VGR3250 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3250 gene: VGAM2539 host target protein and VGAM2540 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2539 and VGAM2540. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3251(VGR3251) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5604] VGR3251 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3251 gene was detected is described hereinabove with reference to Figs.

1-9.

[5605] VGR3251 gene encodes VGR3251 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5606] VGR3251 precursor RNA folds spatially, forming VGR3251 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3251 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3251 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5607] VGR3251 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2541 precursor RNA, VGAM2542 precursor RNA, VGAM2543 precursor RNA, VGAM2544 precursor RNA, VGAM2545 precursor RNA, VGAM2546 precursor RNA and VGAM2547 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM

precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5608] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2541 RNA, VGAM2542 RNA, VGAM2543 RNA, VGAM2544 RNA, VGAM2545 RNA, VGAM2546 RNA and VGAM2547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5609] VGAM2541 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2541 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2541 host target RNA into VGAM2541 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5610] VGAM2542 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2542 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2542 host target RNA into VGAM2542 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5611] VGAM2543 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2543 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2543 host target RNA into VGAM2543 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5612] VGAM2544 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2544 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2544 host target RNA into VGAM2544 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5613] VGAM2545 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2545 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2545 host target RNA into VGAM2545 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5614] VGAM2546 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2546 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2546 host target RNA into VGAM2546 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5615] VGAM2547 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2547 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2547 host target RNA into

VGAM2547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5616] It is appreciated that a function of VGR3251 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3251 gene include diagnosis, prevention and treatment of viral infection by Langat Virus. Specific functions, and accordingly utilities, of VGR3251 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3251 gene: VGAM2541 host target protein, VGAM2542 host target protein, VGAM2543 host target protein, VGAM2544 host target protein, VGAM2545 host target protein, VGAM2546 host target protein and VGAM2547 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2541, VGAM2542, VGAM2543, VGAM2544, VGAM2545, VGAM2546 and VGAM2547. Fig. 9 further provides a conceptual description of novel bioinformati-

cally detected regulatory viral gene, referred to here as Viral Genomic Record 3252(VGR3252) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5617] VGR3252 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3252 gene was detected is described hereinabove with reference to Figs. 1-9.

[5618] VGR3252 gene encodes VGR3252 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5619] VGR3252 precursor RNA folds spatially, forming VGR3252 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3252 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3252 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[5620] VGR3252 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2548 precursor RNA, VGAM2549 precursor RNA and VGAM2550 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5621] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2548 RNA, VGAM2549 RNA and VGAM2550 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5622] VGAM2548 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2548 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2548 host target RNA into VGAM2548 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5623] VGAM2549 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2549 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2549 host target RNA into VGAM2549 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5624] VGAM2550 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2550 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2550 host target RNA into VGAM2550 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5625] It is appreciated that a function of VGR3252 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3252 gene include diagnosis, prevention and treatment of viral infection by Saccharomyces Cerevisiae Virus L-A. Specific functions, and accordingly utilities, of VGR3252 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3252 gene: VGAM2548 host target protein, VGAM2549 host target protein and VGAM2550 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with refer-

ence to VGAM2548, VGAM2549 and VGAM2550. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3253 (VGR3253) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5626] VGR3253 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3253 gene was detected is described hereinabove with reference to Figs. 1-9.

[5627] VGR3253 gene encodes VGR3253 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5628] VGR3253 precursor RNA folds spatially, forming VGR3253 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3253 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of

VGR3253 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5629] VGR3253 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2552 precursor RNA and VGAM2553 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5630] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2552 RNA and VGAM2553 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5631] VGAM2552 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2552 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2552 host target RNA into VGAM2552 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5632] VGAM2553 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2553 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2553 host target RNA into VGAM2553 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5633] It is appreciated that a function of VGR3253 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attack–

ing a host. Accordingly, utilities of VGR3253 gene include diagnosis, prevention and treatment of viral infection by Rice Ragged Stunt Virus. Specific functions, and accordingly utilities, of VGR3253 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3253 gene: VGAM2552 host target protein and VGAM2553 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2552 and VGAM2553. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3254(VGR3254) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5634] VGR3254 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3254 gene was

detected is described hereinabove with reference to Figs. 1-9.

[5635] VGR3254 gene encodes VGR3254 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5636] VGR3254 precursor RNA folds spatially, forming VGR3254 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3254 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3254 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5637] VGR3254 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2554 precursor RNA, VGAM2555 precursor RNA and VGAM2556 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5638] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2554 RNA, VGAM2555 RNA and VGAM2556 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5639] VGAM2554 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2554 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2554 host target RNA into VGAM2554 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5640] VGAM2555 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2555 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2555 host target RNA into VGAM2555 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5641] VGAM2556 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2556 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2556 host target RNA into VGAM2556 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5642] It is appreciated that a function of VGR3254 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3254 gene include diagnosis, prevention and treatment of viral infection by Plautia Stali Intestine Virus. Specific functions, and accordingly utilities, of VGR3254 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3254 gene: VGAM2554 host target protein, VGAM2555 host target protein and VGAM2556 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2554, VGAM2555 and VGAM2556. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3255(VGR3255) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5643] VGR3255 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3255 gene was detected is described hereinabove with reference to Figs. 1–9.

[5644] VGR3255 gene encodes VGR3255 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5645] VGR3255 precursor RNA folds spatially, forming VGR3255 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3255 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3255 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed–reversed sequence of the second half thereof, as is well known in the art.

[5646] VGR3255 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2557 precursor RNA, VGAM2558 precursor RNA, VGAM2559 precursor RNA, VGAM2560

precursor RNA, VGAM2561 precursor RNA, VGAM2562 precursor RNA and VGAM2563 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5647] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2557 RNA, VGAM2558 RNA, VGAM2559 RNA, VGAM2560 RNA, VGAM2561 RNA, VGAM2562 RNA and VGAM2563 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5648] VGAM2557 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2557 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2557 host target RNA into VGAM2557 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5649] VGAM2558 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2558 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2558 host target RNA into VGAM2558 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5650] VGAM2559 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2559 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2559 host target RNA into VGAM2559 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5651] VGAM2560 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2560 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2560 host target RNA into VGAM2560 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5652] VGAM2561 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2561 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2561 host target RNA into VGAM2561 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5653] VGAM2562 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2562 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2562 host target RNA into VGAM2562 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5654] VGAM2563 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2563 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2563 host target RNA into VGAM2563 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5655] It is appreciated that a function of VGR3255 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3255 gene include diagnosis, prevention and treatment of viral infection by Himetobi P Virus. Specific functions, and accordingly utilities, of VGR3255 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3255 gene: VGAM2557 host target protein, VGAM2558 host target protein, VGAM2559 host target protein, VGAM2560 host target protein, VGAM2561 host target protein, VGAM2562 host target protein and VGAM2563 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The func-

tion of these host target genes is elaborated hereinabove with reference to VGAM2557, VGAM2558, VGAM2559, VGAM2560, VGAM2561, VGAM2562 and VGAM2563. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3256(VGR3256) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5656] VGR3256 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3256 gene was detected is described hereinabove with reference to Figs. 1-9.

[5657] VGR3256 gene encodes VGR3256 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5658] VGR3256 precursor RNA folds spatially, forming VGR3256 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3256 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3256 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5659] VGR3256 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2564 precursor RNA, VGAM2565 precursor RNA, VGAM2566 precursor RNA, VGAM2567 precursor RNA, VGAM2568 precursor RNA, VGAM2569 precursor RNA, VGAM2570 precursor RNA and VGAM2571 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5660] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2564 RNA, VGAM2565 RNA, VGAM2566 RNA, VGAM2567 RNA, VGAM2568 RNA, VGAM2569 RNA, VGAM2570 RNA and

VGAM2571 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5661] VGAM2564 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2564 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2564 host target RNA into VGAM2564 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5662] VGAM2565 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2565 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2565 host target RNA into VGAM2565 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5663] VGAM2566 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2566 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2566 host target RNA into VGAM2566 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5664] VGAM2567 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2567 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2567 host target RNA into VGAM2567 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5665] VGAM2568 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2568 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2568 host target RNA into VGAM2568 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5666] VGAM2569 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2569 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2569 host target RNA into VGAM2569 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5667] VGAM2570 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2570 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2570 host target RNA into VGAM2570 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5668] VGAM2571 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2571 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2571 host target RNA into VGAM2571 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5669] It is appreciated that a function of VGR3256 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3256 gene include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGR3256 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3256 gene: VGAM2564 host target protein, VGAM2565 host target protein, VGAM2566 host target protein, VGAM2567 host target protein, VGAM2568 host target protein, VGAM2569 host target protein, VGAM2570 host target protein and VGAM2571 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST

TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2564, VGAM2565, VGAM2566, VGAM2567, VGAM2568, VGAM2569, VGAM2570 and VGAM2571. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3257 (VGR3257) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5670] VGR3257 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3257 gene was detected is described hereinabove with reference to Figs. 1-9.

[5671] VGR3257 gene encodes VGR3257 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5672] VGR3257 precursor RNA folds spatially, forming VGR3257 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3257 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3257 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5673] VGR3257 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2572 precursor RNA, VGAM2573 precursor RNA, VGAM2574 precursor RNA, VGAM2575 precursor RNA, VGAM2576 precursor RNA, VGAM2577 precursor RNA and VGAM2578 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5674] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2572 RNA, VGAM2573 RNA, VGAM2574 RNA, VGAM2575 RNA, VGAM2576 RNA, VGAM2577 RNA and VGAM2578 RNA,

herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5675] VGAM2572 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2572 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2572 host target RNA into VGAM2572 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5676] VGAM2573 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2573 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2573 host target RNA into VGAM2573 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5677] VGAM2574 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2574 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2574 host target RNA into VGAM2574 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5678] VGAM2575 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2575 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2575 host target RNA into VGAM2575 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5679] VGAM2576 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2576 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2576 host target RNA into VGAM2576 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5680] VGAM2577 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2577 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2577 host target RNA into VGAM2577 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5681] VGAM2578 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2578 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2578 host target RNA into VGAM2578 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5682] It is appreciated that a function of VGR3257 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3257 gene include diagnosis, prevention and treatment of viral infection by

Triatoma Virus. Specific functions, and accordingly utilities, of VGR3257 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3257 gene: VGAM2572 host target protein, VGAM2573 host target protein, VGAM2574 host target protein, VGAM2575 host target protein, VGAM2576 host target protein, VGAM2577 host target protein and VGAM2578 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2572, VGAM2573, VGAM2574, VGAM2575, VGAM2576, VGAM2577 and VGAM2578. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3258(VGR3258) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5683] VGR3258 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3258 gene was detected is described hereinabove with reference to Figs. 1-9.

[5684] VGR3258 gene encodes VGR3258 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5685] VGR3258 precursor RNA folds spatially, forming VGR3258 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3258 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3258 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5686] VGR3258 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2579 precursor RNA, VGAM2580 precursor RNA, VGAM2581 precursor RNA, VGAM2582 precursor RNA and VGAM2583 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5687] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2579 RNA, VGAM2580 RNA, VGAM2581 RNA, VGAM2582 RNA and VGAM2583 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5688] VGAM2579 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2579 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2579 host target RNA into VGAM2579 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5689] VGAM2580 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2580 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2580 host target RNA into VGAM2580 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5690] VGAM2581 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2581 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2581 host target RNA into VGAM2581 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5691] VGAM2582 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2582 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2582 host target RNA into VGAM2582 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5692] VGAM2583 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2583 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2583 host target RNA into

VGAM2583 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5693] It is appreciated that a function of VGR3258 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3258 gene include diagnosis, prevention and treatment of viral infection by Triatoma Virus. Specific functions, and accordingly utilities, of VGR3258 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3258 gene: VGAM2579 host target protein, VGAM2580 host target protein, VGAM2581 host target protein, VGAM2582 host target protein and VGAM2583 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2579, VGAM2580, VGAM2581, VGAM2582 and VGAM2583. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record

3259(VGR3259) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[5694] VGR3259 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3259 gene was
detected is described hereinabove with reference to Figs.
1-9.

[5695] VGR3259 gene encodes VGR3259 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[5696] VGR3259 precursor RNA folds spatially, forming VGR3259
folded precursor RNA, herein designated VGR FOLDED
PRECURSOR RNA. It is appreciated that VGR3259 folded
precursor RNA comprises a plurality of what is known in
the art as `hairpin` structures. These `hairpin` structures
are due to the fact that the nucleotide sequence of
VGR3259 precursor RNA comprises a plurality of seg-
ments, the first half of each such segment having a nu-
cleotide sequence which is at least a partial inversed-re-
versed sequence of the second half thereof, as is well

known in the art.

[5697] VGR3259 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2584 precursor RNA, VGAM2585 precursor RNA, VGAM2586 precursor RNA, VGAM2587 precursor RNA and VGAM2588 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5698] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2584 RNA, VGAM2585 RNA, VGAM2586 RNA, VGAM2587 RNA and VGAM2588 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5699] VGAM2584 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2584 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2584 host target RNA into VGAM2584 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5700] VGAM2585 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2585 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2585 host target RNA into VGAM2585 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5701] VGAM2586 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2586 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2586 host target RNA into VGAM2586 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5702] VGAM2587 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2587 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2587 host target RNA into VGAM2587 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5703] VGAM2588 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2588 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2588 host target RNA into VGAM2588 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5704] It is appreciated that a function of VGR3259 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3259 gene include diagnosis, prevention and treatment of viral infection by Satsuma Dwarf Virus. Specific functions, and accordingly utilities, of VGR3259 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3259 gene: VGAM2584 host target protein, VGAM2585 host target protein, VGAM2586 host target protein, VGAM2587 host target protein and VGAM2588 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2584, VGAM2585, VGAM2586, VGAM2587 and VGAM2588. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3260(VGR3260) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5705] VGR3260 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3260 gene was detected is described hereinabove with reference to Figs. 1-9.

[5706] VGR3260 gene encodes VGR3260 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5707] VGR3260 precursor RNA folds spatially, forming VGR3260 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3260 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3260 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5708] VGR3260 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2589 precursor RNA, VGAM2590 precursor RNA, VGAM2591 precursor RNA, VGAM2592 precursor RNA, VGAM2593 precursor RNA, VGAM2594 precursor RNA and VGAM2595 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5709] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2589 RNA, VGAM2590 RNA, VGAM2591 RNA, VGAM2592 RNA, VGAM2593 RNA, VGAM2594 RNA and VGAM2595 RNA,

herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5710] VGAM2589 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2589 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2589 host target RNA into VGAM2589 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5711] VGAM2590 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2590 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2590 host target RNA into VGAM2590 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5712] VGAM2591 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2591 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2591 host target RNA into VGAM2591 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5713] VGAM2592 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2592 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2592 host target RNA into VGAM2592 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5714] VGAM2593 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2593 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2593 host target RNA into VGAM2593 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5715] VGAM2594 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2594 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2594 host target RNA into VGAM2594 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5716] VGAM2595 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2595 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2595 host target RNA into VGAM2595 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5717] It is appreciated that a function of VGR3260 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3260 gene include diagnosis, prevention and treatment of viral infection by

Apple Latent Spherical Virus. Specific functions, and accordingly utilities, of VGR3260 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3260 gene: VGAM2589 host target protein, VGAM2590 host target protein, VGAM2591 host target protein, VGAM2592 host target protein, VGAM2593 host target protein, VGAM2594 host target protein and VGAM2595 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2589, VGAM2590, VGAM2591, VGAM2592, VGAM2593, VGAM2594 and VGAM2595. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3261(VGR3261) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5718] VGR3261 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3261 gene was detected is described hereinabove with reference to Figs. 1-9.

[5719] VGR3261 gene encodes VGR3261 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5720] VGR3261 precursor RNA folds spatially, forming VGR3261 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3261 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3261 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5721] VGR3261 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2596 precursor RNA, VGAM2597 precursor RNA and VGAM2598 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5722] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2596 RNA, VGAM2597 RNA and VGAM2598 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5723] VGAM2596 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2596 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2596 host target RNA into VGAM2596 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5724] VGAM2597 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2597 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2597 host target RNA into VGAM2597 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5725] VGAM2598 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2598 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2598 host target RNA into VGAM2598 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5726] It is appreciated that a function of VGR3261 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3261 gene include diagnosis, prevention and treatment of viral infection by Tobacco Rattle Virus. Specific functions, and accordingly utilities, of VGR3261 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3261 gene: VGAM2596 host target protein, VGAM2597 host target protein and VGAM2598 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2596, VGAM2597 and VGAM2598. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3262(VGR3262) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[5727] VGR3262 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3262 gene was detected is described hereinabove with reference to Figs. 1-9.

[5728] VGR3262 gene encodes VGR3262 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5729] VGR3262 precursor RNA folds spatially, forming VGR3262 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3262 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3262 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5730] VGR3262 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM

precursor RNAs, VGAM2599 precursor RNA, VGAM2600 precursor RNA, VGAM2601 precursor RNA and VGAM2602 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5731] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2599 RNA, VGAM2600 RNA, VGAM2601 RNA and VGAM2602 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5732] VGAM2599 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2599 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2599 host target RNA into

VGAM2599 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5733] VGAM2600 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2600 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2600 host target RNA into VGAM2600 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5734] VGAM2601 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2601 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2601 host target RNA into VGAM2601 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5735] VGAM2602 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2602 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2602 host target RNA into VGAM2602 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5736] It is appreciated that a function of VGR3262 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3262 gene include diagnosis, prevention and treatment of viral infection by Obuda Pepper Virus. Specific functions, and accordingly utilities, of VGR3262 gene correlate with, and may be de-

duced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3262 gene: VGAM2599 host target protein, VGAM2600 host target protein, VGAM2601 host target protein and VGAM2602 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2599, VGAM2600, VGAM2601 and VGAM2602. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3263(VGR3263) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5737] VGR3263 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3263 gene was detected is described hereinabove with reference to Figs. 1-9.

[5738] VGR3263 gene encodes VGR3263 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5739] VGR3263 precursor RNA folds spatially, forming VGR3263 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3263 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3263 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5740] VGR3263 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2603 precursor RNA and VGAM2604 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5741] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2603 RNA and VGAM2604 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5742] VGAM2603 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2603 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2603 host target RNA into VGAM2603 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5743] VGAM2604 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2604 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2604 host target RNA into VGAM2604 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5744] It is appreciated that a function of VGR3263 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3263 gene include diagnosis, prevention and treatment of viral infection by Sugarcane Striate Mosaic Associated Virus. Specific functions, and accordingly utilities, of VGR3263 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3263 gene: VGAM2603 host target protein and VGAM2604 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2603 and VGAM2604. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record

3264(VGR3264) viral gene, which encodes an
`operon-like` cluster of novel viral micro RNA-like genes,
each of which in turn modulates expression of at least one
host target gene, the function and utility of which at least
one host target gene is known in the art.

[5745] VGR3264 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3264 gene was
detected is described hereinabove with reference to Figs.
1-9.

[5746] VGR3264 gene encodes VGR3264 precursor RNA, herein
designated VGR PRECURSOR RNA, an RNA molecule, typi-
cally several hundred nucleotides long.

[5747] VGR3264 precursor RNA folds spatially, forming VGR3264
folded precursor RNA, herein designated VGR FOLDED
PRECURSOR RNA. It is appreciated that VGR3264 folded
precursor RNA comprises a plurality of what is known in
the art as `hairpin` structures. These `hairpin` structures
are due to the fact that the nucleotide sequence of
VGR3264 precursor RNA comprises a plurality of seg-
ments, the first half of each such segment having a nu-
cleotide sequence which is at least a partial inversed-re-
versed sequence of the second half thereof, as is well

known in the art.

[5748] VGR3264 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2605 precursor RNA and VGAM2606 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5749] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2605 RNA and VGAM2606 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5750] VGAM2605 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2605 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2605 host target RNA into VGAM2605 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5751] VGAM2606 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2606 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2606 host target RNA into VGAM2606 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5752] It is appreciated that a function of VGR3264 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3264 gene include diagnosis, prevention and treatment of viral infection by Salmon Pancreas Disease Virus. Specific functions, and accordingly utilities, of VGR3264 gene correlate with, and

may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3264 gene: VGAM2605 host target protein and VGAM2606 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2605 and VGAM2606. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3265(VGR3265) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5753] VGR3265 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3265 gene was detected is described hereinabove with reference to Figs. 1-9.

[5754] VGR3265 gene encodes VGR3265 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[5755] VGR3265 precursor RNA folds spatially, forming VGR3265 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3265 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3265 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5756] VGR3265 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2607 precursor RNA, VGAM2608 precursor RNA, VGAM2609 precursor RNA and VGAM2610 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5757] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2607 RNA, VGAM2608 RNA, VGAM2609 RNA and VGAM2610 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5758] VGAM2607 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2607 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2607 host target RNA into VGAM2607 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5759] VGAM2608 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2608 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2608 host target RNA into VGAM2608 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5760] VGAM2609 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2609 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2609 host target RNA into VGAM2609 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5761] VGAM2610 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2610 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2610 host target RNA into VGAM2610 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5762] It is appreciated that a function of VGR3265 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3265 gene include diagnosis, prevention and treatment of viral infection by Ljungan Virus. Specific functions, and accordingly utilities, of VGR3265 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3265 gene: VGAM2607 host target protein, VGAM2608 host target protein, VGAM2609 host target protein and VGAM2610 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2607, VGAM2608, VGAM2609 and

VGAM2610. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3266 (VGR3266) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5763] VGR3266 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3266 gene was detected is described hereinabove with reference to Figs. 1-9.

[5764] VGR3266 gene encodes VGR3266 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5765] VGR3266 precursor RNA folds spatially, forming VGR3266 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3266 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3266 precursor RNA comprises a plurality of seg-

ments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5766] VGR3266 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2611 precursor RNA and VGAM2612 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5767] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2611 RNA and VGAM2612 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5768] VGAM2611 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2611 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2611 host target RNA into VGAM2611 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5769] VGAM2612 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2612 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2612 host target RNA into VGAM2612 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5770] It is appreciated that a function of VGR3266 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3266 gene include

diagnosis, prevention and treatment of viral infection by Equine Rhinitis A Virus. Specific functions, and accordingly utilities, of VGR3266 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3266 gene: VGAM2611 host target protein and VGAM2612 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2611 and VGAM2612. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3267(VGR3267) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5771] VGR3267 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3267 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5772] VGR3267 gene encodes VGR3267 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5773] VGR3267 precursor RNA folds spatially, forming VGR3267 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3267 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3267 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5774] VGR3267 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2614 precursor RNA, VGAM2615 precursor RNA, VGAM2616 precursor RNA, VGAM2617 precursor RNA, VGAM2618 precursor RNA and VGAM2619 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a

hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5775] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2614 RNA, VGAM2615 RNA, VGAM2616 RNA, VGAM2617 RNA, VGAM2618 RNA and VGAM2619 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5776] VGAM2614 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2614 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2614 host target RNA into VGAM2614 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5777] VGAM2615 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2615 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2615 host target RNA into VGAM2615 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5778] VGAM2616 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2616 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2616 host target RNA into VGAM2616 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5779] VGAM2617 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2617 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2617 host target RNA into VGAM2617 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5780] VGAM2618 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2618 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2618 host target RNA into VGAM2618 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5781] VGAM2619 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2619 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2619 host target RNA into VGAM2619 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5782] It is appreciated that a function of VGR3267 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3267 gene include diagnosis, prevention and treatment of viral infection by Equine Rhinitis B Virus. Specific functions, and accordingly utilities, of VGR3267 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3267 gene: VGAM2614 host

target protein, VGAM2615 host target protein, VGAM2616 host target protein, VGAM2617 host target protein, VGAM2618 host target protein and VGAM2619 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2614, VGAM2615, VGAM2616, VGAM2617, VGAM2618 and VGAM2619. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3268(VGR3268) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5783] VGR3268 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3268 gene was detected is described hereinabove with reference to Figs. 1-9.

[5784] VGR3268 gene encodes VGR3268 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[5785] VGR3268 precursor RNA folds spatially, forming VGR3268 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3268 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3268 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5786] VGR3268 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2620 precursor RNA, VGAM2621 precursor RNA and VGAM2622 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5787] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2620 RNA, VGAM2621 RNA and VGAM2622 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5788] VGAM2620 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2620 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2620 host target RNA into VGAM2620 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5789] VGAM2621 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2621 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2621 host target RNA into VGAM2621 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5790] VGAM2622 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2622 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2622 host target RNA into VGAM2622 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5791] It is appreciated that a function of VGR3268 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3268 gene include diagnosis, prevention and treatment of viral infection by

Porcine Enterovirus A (PEV8). Specific functions, and accordingly utilities, of VGR3268 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3268 gene: VGAM2620 host target protein, VGAM2621 host target protein and VGAM2622 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2620, VGAM2621 and VGAM2622. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3269(VGR3269) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5792] VGR3269 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3269 gene was detected is described hereinabove with reference to Figs.

1-9.

[5793] VGR3269 gene encodes VGR3269 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5794] VGR3269 precursor RNA folds spatially, forming VGR3269 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3269 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3269 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5795] VGR3269 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2623 precursor RNA, VGAM2624 precursor RNA and VGAM2625 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[5796] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2623 RNA, VGAM2624 RNA and VGAM2625 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5797] VGAM2623 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2623 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2623 host target RNA into VGAM2623 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5798] VGAM2624 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2624 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2624 host target RNA into VGAM2624 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5799] VGAM2625 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2625 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2625 host target RNA into VGAM2625 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5800] It is appreciated that a function of VGR3269 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3269 gene include diagnosis, prevention and treatment of viral infection by A-2 Plaque Virus. Specific functions, and accordingly utilities, of VGR3269 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3269 gene: VGAM2623 host target protein, VGAM2624 host target protein and VGAM2625 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2623, VGAM2624 and VGAM2625. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3270(VGR3270) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5801] VGR3270 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3270 gene was detected is described hereinabove with reference to Figs. 1-9.

[5802] VGR3270 gene encodes VGR3270 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5803] VGR3270 precursor RNA folds spatially, forming VGR3270 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3270 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3270 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5804] VGR3270 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2626 precursor RNA, VGAM2627 precursor RNA, VGAM2628 precursor RNA and VGAM2629 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5805] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2626 RNA, VGAM2627 RNA, VGAM2628 RNA and VGAM2629 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5806] VGAM2626 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2626 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2626 host target RNA into VGAM2626 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5807] VGAM2627 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2627 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2627 host target RNA into VGAM2627 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5808] VGAM2628 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2628 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2628 host target RNA into VGAM2628 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5809] VGAM2629 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2629 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2629 host target RNA into VGAM2629 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5810] It is appreciated that a function of VGR3270 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3270 gene include diagnosis, prevention and treatment of viral infection by Avian Encephalomyelitis Virus. Specific functions, and accordingly utilities, of VGR3270 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3270 gene: VGAM2626

host target protein, VGAM2627 host target protein, VGAM2628 host target protein and VGAM2629 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2626, VGAM2627, VGAM2628 and VGAM2629. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3271(VGR3271) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5811] VGR3271 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3271 gene was detected is described hereinabove with reference to Figs. 1-9.

[5812] VGR3271 gene encodes VGR3271 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5813] VGR3271 precursor RNA folds spatially, forming VGR3271

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3271 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3271 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5814] VGR3271 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2630 precursor RNA, VGAM2631 precursor RNA, VGAM2632 precursor RNA, VGAM2633 precursor RNA, VGAM2634 precursor RNA and VGAM2635 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5815] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2630

RNA, VGAM2631 RNA, VGAM2632 RNA, VGAM2633 RNA, VGAM2634 RNA and VGAM2635 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5816] VGAM2630 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2630 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2630 host target RNA into VGAM2630 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5817] VGAM2631 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2631 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2631 host target RNA into VGAM2631 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5818] VGAM2632 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2632 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2632 host target RNA into VGAM2632 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5819] VGAM2633 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2633 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2633 host target RNA into VGAM2633 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5820] VGAM2634 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2634 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2634 host target RNA into VGAM2634 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5821] VGAM2635 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2635 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2635 host target RNA into VGAM2635 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5822] It is appreciated that a function of VGR3271 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3271 gene include diagnosis, prevention and treatment of viral infection by Tamana Bat Virus. Specific functions, and accordingly utilities, of VGR3271 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3271 gene: VGAM2630 host target protein, VGAM2631 host target protein, VGAM2632 host target protein, VGAM2633 host target protein, VGAM2634 host target protein and VGAM2635 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN.

The function of these host target genes is elaborated hereinabove with reference to VGAM2630, VGAM2631, VGAM2632, VGAM2633, VGAM2634 and VGAM2635. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3272(VGR3272) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5823] VGR3272 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3272 gene was detected is described hereinabove with reference to Figs. 1-9.

[5824] VGR3272 gene encodes VGR3272 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5825] VGR3272 precursor RNA folds spatially, forming VGR3272 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3272 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3272 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5826] VGR3272 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2636 precursor RNA and VGAM2637 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5827] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2636 RNA and VGAM2637 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5828] VGAM2636 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2636 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2636 host target RNA into VGAM2636 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5829] VGAM2637 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2637 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2637 host target RNA into VGAM2637 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5830] It is appreciated that a function of VGR3272 gene, herein

designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3272 gene include diagnosis, prevention and treatment of viral infection by Sheeppox Virus. Specific functions, and accordingly utilities, of VGR3272 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3272 gene: VGAM2636 host target protein and VGAM2637 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2636 and VGAM2637. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3273(VGR3273) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5831] VGR3273 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3273 gene was detected is described hereinabove with reference to Figs. 1-9.

[5832] VGR3273 gene encodes VGR3273 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5833] VGR3273 precursor RNA folds spatially, forming VGR3273 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3273 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3273 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5834] VGR3273 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2638 precursor RNA, VGAM2639 precursor RNA, VGAM2640 precursor RNA, VGAM2641 precursor RNA and VGAM2642 precursor RNA, herein

schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5835] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2638 RNA, VGAM2639 RNA, VGAM2640 RNA, VGAM2641 RNA and VGAM2642 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5836] VGAM2638 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2638 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2638 host target RNA into VGAM2638 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5837] VGAM2639 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2639 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2639 host target RNA into VGAM2639 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5838] VGAM2640 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2640 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2640 host target RNA into VGAM2640 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5839] VGAM2641 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2641 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2641 host target RNA into VGAM2641 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5840] VGAM2642 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2642 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2642 host target RNA into

VGAM2642 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5841] It is appreciated that a function of VGR3273 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3273 gene include diagnosis, prevention and treatment of viral infection by Foot-and-mouth Disease Virus O. Specific functions, and accordingly utilities, of VGR3273 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3273 gene: VGAM2638 host target protein, VGAM2639 host target protein, VGAM2640 host target protein, VGAM2641 host target protein and VGAM2642 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2638, VGAM2639, VGAM2640, VGAM2641 and VGAM2642. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic

Record 3274(VGR3274) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5842] VGR3274 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3274 gene was detected is described hereinabove with reference to Figs. 1-9.

[5843] VGR3274 gene encodes VGR3274 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5844] VGR3274 precursor RNA folds spatially, forming VGR3274 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3274 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3274 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[5845] VGR3274 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2643 precursor RNA, VGAM2644 precursor RNA, VGAM2645 precursor RNA, VGAM2646 precursor RNA, VGAM2647 precursor RNA, VGAM2648 precursor RNA and VGAM2649 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5846] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2643 RNA, VGAM2644 RNA, VGAM2645 RNA, VGAM2646 RNA, VGAM2647 RNA, VGAM2648 RNA and VGAM2649 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5847] VGAM2643 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2643 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2643 host target RNA into VGAM2643 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5848] VGAM2644 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2644 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2644 host target RNA into VGAM2644 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5849] VGAM2645 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2645 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2645 host target RNA into VGAM2645 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5850] VGAM2646 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2646 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2646 host target RNA into VGAM2646 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5851] VGAM2647 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2647 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2647 host target RNA into VGAM2647 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5852] VGAM2648 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2648 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2648 host target RNA into VGAM2648 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5853] VGAM2649 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2649 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2649 host target RNA into VGAM2649 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5854] It is appreciated that a function of VGR3274 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3274 gene include diagnosis, prevention and treatment of viral infection by Cowpea Aphid-borne Mosaic Virus. Specific functions, and accordingly utilities, of VGR3274 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3274 gene: VGAM2643 host target protein, VGAM2644 host target protein,

VGAM2645 host target protein, VGAM2646 host target protein, VGAM2647 host target protein, VGAM2648 host target protein and VGAM2649 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2643, VGAM2644, VGAM2645, VGAM2646, VGAM2647, VGAM2648 and VGAM2649. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3275(VGR3275) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5855] VGR3275 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3275 gene was detected is described hereinabove with reference to Figs. 1-9.

[5856] VGR3275 gene encodes VGR3275 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[5857] VGR3275 precursor RNA folds spatially, forming VGR3275 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3275 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3275 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5858] VGR3275 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2650 precursor RNA and VGAM2651 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5859] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2650

RNA and VGAM2651 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5860] VGAM2650 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2650 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2650 host target RNA into VGAM2650 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5861] VGAM2651 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2651 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2651 host target RNA into VGAM2651 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5862] It is appreciated that a function of VGR3275 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3275 gene include diagnosis, prevention and treatment of viral infection by Trichomonas Vaginalis Virus 3. Specific functions, and accordingly utilities, of VGR3275 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3275 gene: VGAM2650 host target protein and VGAM2651 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2650 and VGAM2651. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3276(VGR3276) viral gene, which encodes an `operon-like` cluster of novel viral mi-

cro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5863] VGR3276 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3276 gene was detected is described hereinabove with reference to Figs. 1-9.

[5864] VGR3276 gene encodes VGR3276 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5865] VGR3276 precursor RNA folds spatially, forming VGR3276 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3276 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3276 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5866] VGR3276 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2652 precursor RNA, VGAM2653 precursor RNA, VGAM2654 precursor RNA and VGAM2655 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5867] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2652 RNA, VGAM2653 RNA, VGAM2654 RNA and VGAM2655 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5868] VGAM2652 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2652 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2652 host target RNA into VGAM2652 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5869] VGAM2653 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2653 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2653 host target RNA into VGAM2653 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5870] VGAM2654 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2654 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2654 host target RNA into VGAM2654 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5871] VGAM2655 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2655 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2655 host target RNA into VGAM2655 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5872] It is appreciated that a function of VGR3276 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3276 gene include diagnosis, prevention and treatment of viral infection by

Sorghum Mosaic Virus. Specific functions, and accordingly utilities, of VGR3276 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3276 gene: VGAM2652 host target protein, VGAM2653 host target protein, VGAM2654 host target protein and VGAM2655 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2652, VGAM2653, VGAM2654 and VGAM2655. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3277(VGR3277) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5873] VGR3277 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3277 gene was detected is described hereinabove with reference to Figs.

1-9.

- [5874] VGR3277 gene encodes VGR3277 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.
- [5875] VGR3277 precursor RNA folds spatially, forming VGR3277 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3277 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3277 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.
- [5876] VGR3277 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 8 separate VGAM precursor RNAs, VGAM2656 precursor RNA, VGAM2657 precursor RNA, VGAM2658 precursor RNA, VGAM2659 precursor RNA, VGAM2660 precursor RNA, VGAM2661 precursor RNA, VGAM2662 precursor RNA and VGAM2663 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED

PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5877] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2656 RNA, VGAM2657 RNA, VGAM2658 RNA, VGAM2659 RNA, VGAM2660 RNA, VGAM2661 RNA, VGAM2662 RNA and VGAM2663 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5878] VGAM2656 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2656 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2656 host target RNA into VGAM2656 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5879] VGAM2657 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2657 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2657 host target RNA into VGAM2657 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5880] VGAM2658 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2658 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2658 host target RNA into VGAM2658 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5881] VGAM2659 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2659 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2659 host target RNA into VGAM2659 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5882] VGAM2660 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2660 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2660 host target RNA into VGAM2660 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5883] VGAM2661 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2661 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2661 host target RNA into VGAM2661 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5884] VGAM2662 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2662 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2662 host target RNA into

VGAM2662 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5885] VGAM2663 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2663 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2663 host target RNA into VGAM2663 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5886] It is appreciated that a function of VGR3277 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3277 gene include diagnosis, prevention and treatment of viral infection by Potato Virus A. Specific functions, and accordingly utilities, of VGR3277 gene correlate with, and may be deduced from, the identity of the host target genes, which

are inhibited by VGAM RNAs comprised in the
`operon-like` cluster of VGR3277 gene: VGAM2656 host
target protein, VGAM2657 host target protein, VGAM2658
host target protein, VGAM2659 host target protein,
VGAM2660 host target protein, VGAM2661 host target
protein, VGAM2662 host target protein and VGAM2663
host target protein, herein schematically represented by
VGAM1 HOST TARGET PROTEIN through VGAM3 HOST
TARGET PROTEIN. The function of these host target genes
is elaborated hereinabove with reference to VGAM2656,
VGAM2657, VGAM2658, VGAM2659, VGAM2660,
VGAM2661, VGAM2662 and VGAM2663. Fig. 9 further
provides a conceptual description of novel bioinformati-
cally detected regulatory viral gene, referred to here as Vi-
ral Genomic Record 3278(VGR3278) viral gene, which en-
codes an `operon-like` cluster of novel viral micro RNA-
like genes, each of which in turn modulates expression of
at least one host target gene, the function and utility of
which at least one host target gene is known in the art.

[5887] VGR3278 gene, herein designated VGR GENE, is a novel
bioinformatically detected regulatory, non protein coding,
RNA viral gene. The method by which VGR3278 gene was
detected is described hereinabove with reference to Figs.

1-9.

[5888] VGR3278 gene encodes VGR3278 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5889] VGR3278 precursor RNA folds spatially, forming VGR3278 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3278 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3278 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5890] VGR3278 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2664 precursor RNA, VGAM2665 precursor RNA and VGAM2666 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig.

1.

[5891] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2664 RNA, VGAM2665 RNA and VGAM2666 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5892] VGAM2664 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2664 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2664 host target RNA into VGAM2664 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5893] VGAM2665 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2665 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2665 host target RNA into VGAM2665 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5894] VGAM2666 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2666 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2666 host target RNA into VGAM2666 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5895] It is appreciated that a function of VGR3278 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3278 gene include diagnosis, prevention and treatment of viral infection by Cryphonectria Parasitica Mitovirus 1–NB631. Specific functions, and accordingly utilities, of VGR3278 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3278 gene: VGAM2664 host target protein, VGAM2665 host target protein and VGAM2666 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2664, VGAM2665 and VGAM2666. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3279(VGR3279) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5896] VGR3279 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3279 gene was detected is described hereinabove with reference to Figs. 1-9.

[5897] VGR3279 gene encodes VGR3279 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5898] VGR3279 precursor RNA folds spatially, forming VGR3279 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3279 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3279 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5899] VGR3279 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2667 precursor RNA, VGAM2668 precursor RNA, VGAM2669 precursor RNA and VGAM2670 precursor RNA, herein schematically represented by

VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5900] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2667 RNA, VGAM2668 RNA, VGAM2669 RNA and VGAM2670 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5901] VGAM2667 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2667 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2667 host target RNA into VGAM2667 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5902] VGAM2668 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2668 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2668 host target RNA into VGAM2668 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5903] VGAM2669 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2669 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2669 host target RNA into VGAM2669 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5904] VGAM2670 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2670 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2670 host target RNA into VGAM2670 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5905] It is appreciated that a function of VGR3279 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3279 gene include diagnosis, prevention and treatment of viral infection by Bean Common Mosaic Necrosis Virus. Specific functions, and accordingly utilities, of VGR3279 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3279 gene: VGAM2667

host target protein, VGAM2668 host target protein, VGAM2669 host target protein and VGAM2670 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2667, VGAM2668, VGAM2669 and VGAM2670. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3280(VGR3280) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5906] VGR3280 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3280 gene was detected is described hereinabove with reference to Figs. 1-9.

[5907] VGR3280 gene encodes VGR3280 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5908] VGR3280 precursor RNA folds spatially, forming VGR3280

folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3280 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3280 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5909] VGR3280 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2671 precursor RNA, VGAM2672 precursor RNA, VGAM2673 precursor RNA, VGAM2674 precursor RNA, VGAM2675 precursor RNA, VGAM2676 precursor RNA and VGAM2677 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5910] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2671 RNA, VGAM2672 RNA, VGAM2673 RNA, VGAM2674 RNA, VGAM2675 RNA, VGAM2676 RNA and VGAM2677 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5911] VGAM2671 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2671 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2671 host target RNA into VGAM2671 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5912] VGAM2672 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2672 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2672 host target RNA into VGAM2672 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5913] VGAM2673 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2673 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2673 host target RNA into VGAM2673 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5914] VGAM2674 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2674 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2674 host target RNA into VGAM2674 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5915] VGAM2675 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2675 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2675 host target RNA into VGAM2675 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5916] VGAM2676 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2676 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2676 host target RNA into VGAM2676 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5917] VGAM2677 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2677 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2677 host target RNA into VGAM2677 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5918] It is appreciated that a function of VGR3280 gene, herein designated VGR GENE, is inhibition of expression of host

target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3280 gene include diagnosis, prevention and treatment of viral infection by Ophiostoma Mitovirus 3a. Specific functions, and accordingly utilities, of VGR3280 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3280 gene: VGAM2671 host target protein, VGAM2672 host target protein, VGAM2673 host target protein, VGAM2674 host target protein, VGAM2675 host target protein, VGAM2676 host target protein and VGAM2677 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2671, VGAM2672, VGAM2673, VGAM2674, VGAM2675, VGAM2676 and VGAM2677. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3281(VGR3281) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function

and utility of which at least one host target gene is known in the art.

[5919] VGR3281 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3281 gene was detected is described hereinabove with reference to Figs. 1-9.

[5920] VGR3281 gene encodes VGR3281 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5921] VGR3281 precursor RNA folds spatially, forming VGR3281 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3281 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3281 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5922] VGR3281 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM

precursor RNAs, VGAM2678 precursor RNA, VGAM2679 precursor RNA, VGAM2680 precursor RNA, VGAM2681 precursor RNA, VGAM2682 precursor RNA and VGAM2683 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5923] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2678 RNA, VGAM2679 RNA, VGAM2680 RNA, VGAM2681 RNA, VGAM2682 RNA and VGAM2683 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5924] VGAM2678 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2678 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2678 host target RNA into VGAM2678 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5925] VGAM2679 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2679 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2679 host target RNA into VGAM2679 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5926] VGAM2680 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2680 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2680 host target RNA into VGAM2680 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5927] VGAM2681 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2681 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2681 host target RNA into VGAM2681 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5928] VGAM2682 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2682 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2682 host target RNA into VGAM2682 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5929] VGAM2683 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2683 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2683 host target RNA into VGAM2683 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5930] It is appreciated that a function of VGR3281 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3281 gene include

diagnosis, prevention and treatment of viral infection by Ophiostoma Novo-ulmi Mitovirus 4-Ld. Specific functions, and accordingly utilities, of VGR3281 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3281 gene: VGAM2678 host target protein, VGAM2679 host target protein, VGAM2680 host target protein, VGAM2681 host target protein, VGAM2682 host target protein and VGAM2683 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2678, VGAM2679, VGAM2680, VGAM2681, VGAM2682 and VGAM2683. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3282(VGR3282) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5931] VGR3282 gene, herein designated VGR GENE, is a novel

bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3282 gene was detected is described hereinabove with reference to Figs. 1-9.

[5932] VGR3282 gene encodes VGR3282 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5933] VGR3282 precursor RNA folds spatially, forming VGR3282 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3282 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3282 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5934] VGR3282 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2684 precursor RNA, VGAM2685 precursor RNA and VGAM2686 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR

through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5935] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2684 RNA, VGAM2685 RNA and VGAM2686 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5936] VGAM2684 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2684 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2684 host target RNA into VGAM2684 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5937] VGAM2685 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2685 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2685 host target RNA into VGAM2685 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5938] VGAM2686 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2686 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2686 host target RNA into VGAM2686 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5939] It is appreciated that a function of VGR3282 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3282 gene include diagnosis, prevention and treatment of viral infection by Ophiostoma Novo-ulmi Mitovirus 5-Ld. Specific functions, and accordingly utilities, of VGR3282 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3282 gene: VGAM2684 host target protein, VGAM2685 host target protein and VGAM2686 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2684, VGAM2685 and VGAM2686. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3283(VGR3283) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and

utility of which at least one host target gene is known in the art.

[5940] VGR3283 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3283 gene was detected is described hereinabove with reference to Figs. 1-9.

[5941] VGR3283 gene encodes VGR3283 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5942] VGR3283 precursor RNA folds spatially, forming VGR3283 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3283 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3283 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5943] VGR3283 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM

precursor RNAs, VGAM2687 precursor RNA, VGAM2688 precursor RNA and VGAM2689 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5944] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2687 RNA, VGAM2688 RNA and VGAM2689 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5945] VGAM2687 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2687 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2687 host target RNA into

VGAM2687 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5946] VGAM2688 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2688 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2688 host target RNA into VGAM2688 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5947] VGAM2689 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2689 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2689 host target RNA into VGAM2689 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5948] It is appreciated that a function of VGR3283 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3283 gene include diagnosis, prevention and treatment of viral infection by Southern Bean Mosaic Virus. Specific functions, and accordingly utilities, of VGR3283 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3283 gene: VGAM2687 host target protein, VGAM2688 host target protein and VGAM2689 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2687, VGAM2688 and VGAM2689. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3284(VGR3284) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5949] VGR3284 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3284 gene was detected is described hereinabove with reference to Figs. 1-9.

[5950] VGR3284 gene encodes VGR3284 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5951] VGR3284 precursor RNA folds spatially, forming VGR3284 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3284 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3284 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[5952] VGR3284 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 5 separate VGAM precursor RNAs, VGAM2690 precursor RNA, VGAM2691 precursor RNA, VGAM2692 precursor RNA, VGAM2693 precursor RNA and VGAM2694 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5953] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2690 RNA, VGAM2691 RNA, VGAM2692 RNA, VGAM2693 RNA and VGAM2694 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5954] VGAM2690 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2690 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through

VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2690 host target RNA into VGAM2690 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5955] VGAM2691 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2691 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2691 host target RNA into VGAM2691 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5956] VGAM2692 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2692 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2692 host target RNA into VGAM2692 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5957] VGAM2693 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2693 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2693 host target RNA into VGAM2693 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5958] VGAM2694 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2694 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2694 host target RNA into VGAM2694 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5959] It is appreciated that a function of VGR3284 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3284 gene include diagnosis, prevention and treatment of viral infection by Phthorimaea Operculella Granulovirus. Specific functions, and accordingly utilities, of VGR3284 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3284 gene: VGAM2690 host target protein, VGAM2691 host target protein, VGAM2692 host target protein, VGAM2693 host target protein and VGAM2694 host target protein, herein schematically represented by VGAM1 HOST TARGET PRO-

TEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2690, VGAM2691, VGAM2692, VGAM2693 and VGAM2694. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3285 (VGR3285) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5960] VGR3285 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3285 gene was detected is described hereinabove with reference to Figs. 1-9.

[5961] VGR3285 gene encodes VGR3285 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5962] VGR3285 precursor RNA folds spatially, forming VGR3285 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3285 folded precursor RNA comprises a plurality of what is known in

the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3285 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5963] VGR3285 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 4 separate VGAM precursor RNAs, VGAM2696 precursor RNA, VGAM2697 precursor RNA, VGAM2698 precursor RNA and VGAM2699 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5964] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2696 RNA, VGAM2697 RNA, VGAM2698 RNA and VGAM2699 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5965] VGAM2696 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2696 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2696 host target RNA into VGAM2696 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5966] VGAM2697 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2697 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2697 host target RNA into VGAM2697 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5967] VGAM2698 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2698 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2698 host target RNA into VGAM2698 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5968] VGAM2699 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2699 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2699 host target RNA into VGAM2699 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5969] It is appreciated that a function of VGR3285 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3285 gene include diagnosis, prevention and treatment of viral infection by Paprika Mild Mottle Virus. Specific functions, and accordingly utilities, of VGR3285 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3285 gene: VGAM2696 host target protein, VGAM2697 host target protein, VGAM2698 host target protein and VGAM2699 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2696, VGAM2697, VGAM2698 and VGAM2699. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3286(VGR3286) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes,

each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5970] VGR3286 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3286 gene was detected is described hereinabove with reference to Figs. 1-9.

[5971] VGR3286 gene encodes VGR3286 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5972] VGR3286 precursor RNA folds spatially, forming VGR3286 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3286 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3286 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5973] VGR3286 folded precursor RNA is naturally processed by

cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2700 precursor RNA, VGAM2701 precursor RNA and VGAM2702 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5974] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2700 RNA, VGAM2701 RNA and VGAM2702 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5975] VGAM2700 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2700 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2700 host target RNA into VGAM2700 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5976] VGAM2701 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2701 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2701 host target RNA into VGAM2701 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5977] VGAM2702 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2702 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2702 host target RNA into VGAM2702 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5978] It is appreciated that a function of VGR3286 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3286 gene include diagnosis, prevention and treatment of viral infection by La Crosse Virus. Specific functions, and accordingly utilities, of VGR3286 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3286 gene: VGAM2700 host target protein, VGAM2701 host target protein and VGAM2702 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2700, VGAM2701 and VGAM2702. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to

here as Viral Genomic Record 3287(VGR3287) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5979] VGR3287 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3287 gene was detected is described hereinabove with reference to Figs. 1-9.

[5980] VGR3287 gene encodes VGR3287 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5981] VGR3287 precursor RNA folds spatially, forming VGR3287 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3287 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3287 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[5982] VGR3287 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2703 precursor RNA and VGAM2704 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5983] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2703 RNA and VGAM2704 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5984] VGAM2703 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2703 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2703 host target RNA into VGAM2703 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5985] VGAM2704 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2704 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2704 host target RNA into VGAM2704 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5986] It is appreciated that a function of VGR3287 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3287 gene include diagnosis, prevention and treatment of viral infection by Mamestra Configurata Nucleopolyhedrovirus B. Specific

functions, and accordingly utilities, of VGR3287 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3287 gene: VGAM2703 host target protein and VGAM2704 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2703 and VGAM2704. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3288(VGR3288) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5987] VGR3288 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3288 gene was detected is described hereinabove with reference to Figs. 1-9.

[5988] VGR3288 gene encodes VGR3288 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5989] VGR3288 precursor RNA folds spatially, forming VGR3288 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3288 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3288 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[5990] VGR3288 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2706 precursor RNA and VGAM2707 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5991] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2706 RNA and VGAM2707 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[5992] VGAM2706 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2706 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2706 host target RNA into VGAM2706 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5993] VGAM2707 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2707 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2707 host target RNA into VGAM2707 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[5994] It is appreciated that a function of VGR3288 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3288 gene include diagnosis, prevention and treatment of viral infection by Heliothis Zea Virus 1 (HZV-1). Specific functions, and accordingly utilities, of VGR3288 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3288 gene: VGAM2706 host target protein and VGAM2707 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2706 and VGAM2707. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3289(VGR3289) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[5995] VGR3289 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3289 gene was detected is described hereinabove with reference to Figs. 1-9.

[5996] VGR3289 gene encodes VGR3289 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[5997] VGR3289 precursor RNA folds spatially, forming VGR3289 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3289 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3289 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[5998] VGR3289 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2708 precursor RNA and VGAM2709 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[5999] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2708 RNA and VGAM2709 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6000] VGAM2708 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2708 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2708 host target RNA into VGAM2708 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6001] VGAM2709 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2709 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2709 host target RNA into VGAM2709 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6002] It is appreciated that a function of VGR3289 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3289 gene include diagnosis, prevention and treatment of viral infection by Heliothis Zea Virus 1 (HZV-1). Specific functions, and accordingly utilities, of VGR3289 gene correlate with, and

may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3289 gene: VGAM2708 host target protein and VGAM2709 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2708 and VGAM2709. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3290(VGR3290) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6003] VGR3290 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3290 gene was detected is described hereinabove with reference to Figs. 1-9.

[6004] VGR3290 gene encodes VGR3290 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[6005] VGR3290 precursor RNA folds spatially, forming VGR3290 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3290 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3290 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6006] VGR3290 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2711 precursor RNA and VGAM2712 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6007] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2711

RNA and VGAM2712 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6008] VGAM2711 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2711 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2711 host target RNA into VGAM2711 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6009] VGAM2712 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2712 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2712 host target RNA into VGAM2712 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6010] It is appreciated that a function of VGR3290 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3290 gene include diagnosis, prevention and treatment of viral infection by Chikungunya Virus. Specific functions, and accordingly utilities, of VGR3290 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3290 gene: VGAM2711 host target protein and VGAM2712 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2711 and VGAM2712. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3291(VGR3291) viral gene, which encodes an `operon-like` cluster of novel viral micro

RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6011] VGR3291 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3291 gene was detected is described hereinabove with reference to Figs. 1-9.

[6012] VGR3291 gene encodes VGR3291 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6013] VGR3291 precursor RNA folds spatially, forming VGR3291 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3291 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3291 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6014] VGR3291 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 3 separate VGAM precursor RNAs, VGAM2713 precursor RNA, VGAM2714 precursor RNA and VGAM2715 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6015] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2713 RNA, VGAM2714 RNA and VGAM2715 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6016] VGAM2713 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2713 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2713 host target RNA into VGAM2713 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6017] VGAM2714 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2714 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2714 host target RNA into VGAM2714 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6018] VGAM2715 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2715 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2715 host target RNA into VGAM2715 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6019] It is appreciated that a function of VGR3291 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3291 gene include diagnosis, prevention and treatment of viral infection by Mammalian Orthoreovirus 2. Specific functions, and accordingly utilities, of VGR3291 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3291 gene: VGAM2713 host target protein, VGAM2714 host target protein and VGAM2715 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2713, VGAM2714 and VGAM2715. Fig. 9 further provides a conceptual description of novel bioin-

formatically detected regulatory viral gene, referred to here as Viral Genomic Record 3292(VGR3292) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6020] VGR3292 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3292 gene was detected is described hereinabove with reference to Figs. 1-9.

[6021] VGR3292 gene encodes VGR3292 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6022] VGR3292 precursor RNA folds spatially, forming VGR3292 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3292 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3292 precursor RNA comprises a plurality of segments, the first half of each such segment having a nu-

cleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6023] VGR3292 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2717 precursor RNA and VGAM2718 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6024] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2717 RNA and VGAM2718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6025] VGAM2717 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2717 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site

corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2717 host target RNA into VGAM2717 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6026] VGAM2718 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2718 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2718 host target RNA into VGAM2718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6027] It is appreciated that a function of VGR3292 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3292 gene include diagnosis, prevention and treatment of viral infection by

Rachiplusia Ou Multiple Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGR3292 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3292 gene: VGAM2717 host target protein and VGAM2718 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2717 and VGAM2718. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3293(VGR3293) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6028] VGR3293 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3293 gene was detected is described hereinabove with reference to Figs. 1-9.

[6029] VGR3293 gene encodes VGR3293 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6030] VGR3293 precursor RNA folds spatially, forming VGR3293 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3293 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3293 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6031] VGR3293 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 7 separate VGAM precursor RNAs, VGAM2719 precursor RNA, VGAM2720 precursor RNA, VGAM2721 precursor RNA, VGAM2722 precursor RNA, VGAM2723 precursor RNA, VGAM2724 precursor RNA and VGAM2725 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment,

corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6032] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2719 RNA, VGAM2720 RNA, VGAM2721 RNA, VGAM2722 RNA, VGAM2723 RNA, VGAM2724 RNA and VGAM2725 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6033] VGAM2719 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2719 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2719 host target RNA into VGAM2719 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6034] VGAM2720 RNA, herein schematically represented by

VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2720 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2720 host target RNA into VGAM2720 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6035] VGAM2721 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2721 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2721 host target RNA into VGAM2721 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6036] VGAM2722 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2722 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2722 host target RNA into VGAM2722 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6037] VGAM2723 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2723 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2723 host target RNA into VGAM2723 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through

VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6038] VGAM2724 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2724 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2724 host target RNA into VGAM2724 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6039] VGAM2725 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2725 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2725 host target RNA into VGAM2725 host target protein, herein schematically rep-

resented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6040] It is appreciated that a function of VGR3293 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3293 gene include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGR3293 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3293 gene: VGAM2719 host target protein, VGAM2720 host target protein, VGAM2721 host target protein, VGAM2722 host target protein, VGAM2723 host target protein, VGAM2724 host target protein and VGAM2725 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2719, VGAM2720, VGAM2721, VGAM2722, VGAM2723, VGAM2724 and VGAM2725. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred

to here as Viral Genomic Record 3294(VGR3294) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6041] VGR3294 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3294 gene was detected is described hereinabove with reference to Figs. 1-9.

[6042] VGR3294 gene encodes VGR3294 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6043] VGR3294 precursor RNA folds spatially, forming VGR3294 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3294 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3294 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-re-

versed sequence of the second half thereof, as is well known in the art.

[6044] VGR3294 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2726 precursor RNA and VGAM2727 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6045] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2726 RNA and VGAM2727 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6046] VGAM2726 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2726 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2726 host target RNA into VGAM2726 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6047] VGAM2727 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2727 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2727 host target RNA into VGAM2727 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6048] It is appreciated that a function of VGR3294 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3294 gene include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and ac-

cordingly utilities, of VGR3294 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3294 gene: VGAM2726 host target protein and VGAM2727 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2726 and VGAM2727. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3295(VGR3295) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6049] VGR3295 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3295 gene was detected is described hereinabove with reference to Figs. 1-9.

[6050] VGR3295 gene encodes VGR3295 precursor RNA, herein

designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6051] VGR3295 precursor RNA folds spatially, forming VGR3295 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3295 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3295 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6052] VGR3295 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2728 precursor RNA and VGAM2729 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6053] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA

segments of about 22 nucleotides in length, VGAM2728 RNA and VGAM2729 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6054] VGAM2728 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2728 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2728 host target RNA into VGAM2728 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6055] VGAM2729 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2729 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2729 host target RNA into VGAM2729 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6056] It is appreciated that a function of VGR3295 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3295 gene include diagnosis, prevention and treatment of viral infection by Aphid Lethal Paralysis Virus. Specific functions, and accordingly utilities, of VGR3295 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3295 gene: VGAM2728 host target protein and VGAM2729 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated herein-above with reference to VGAM2728 and VGAM2729. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3296(VGR3296) viral gene,

which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6057] VGR3296 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3296 gene was detected is described hereinabove with reference to Figs. 1-9.

[6058] VGR3296 gene encodes VGR3296 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typically several hundred nucleotides long.

[6059] VGR3296 precursor RNA folds spatially, forming VGR3296 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3296 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3296 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well

known in the art.

[6060] VGR3296 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 2 separate VGAM precursor RNAs, VGAM2730 precursor RNA and VGAM2731 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6061] The above mentioned VGAM precursor RNAs are `diced` by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2730 RNA and VGAM2731 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6062] VGAM2730 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2730 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby

inhibiting translation of VGAM2730 host target RNA into VGAM2730 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6063] VGAM2731 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2731 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2731 host target RNA into VGAM2731 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6064] It is appreciated that a function of VGR3296 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3296 gene include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGR3296 gene correlate with, and may

be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3296 gene: VGAM2730 host target protein and VGAM2731 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2730 and VGAM2731. Fig. 9 further provides a conceptual description of novel bioinformatically detected regulatory viral gene, referred to here as Viral Genomic Record 3297(VGR3297) viral gene, which encodes an `operon-like` cluster of novel viral micro RNA-like genes, each of which in turn modulates expression of at least one host target gene, the function and utility of which at least one host target gene is known in the art.

[6065] VGR3297 gene, herein designated VGR GENE, is a novel bioinformatically detected regulatory, non protein coding, RNA viral gene. The method by which VGR3297 gene was detected is described hereinabove with reference to Figs. 1-9.

[6066] VGR3297 gene encodes VGR3297 precursor RNA, herein designated VGR PRECURSOR RNA, an RNA molecule, typi-

cally several hundred nucleotides long.

[6067] VGR3297 precursor RNA folds spatially, forming VGR3297 folded precursor RNA, herein designated VGR FOLDED PRECURSOR RNA. It is appreciated that VGR3297 folded precursor RNA comprises a plurality of what is known in the art as `hairpin` structures. These `hairpin` structures are due to the fact that the nucleotide sequence of VGR3297 precursor RNA comprises a plurality of segments, the first half of each such segment having a nucleotide sequence which is at least a partial inversed-reversed sequence of the second half thereof, as is well known in the art.

[6068] VGR3297 folded precursor RNA is naturally processed by cellular enzymatic activity into at least 6 separate VGAM precursor RNAs, VGAM2733 precursor RNA, VGAM2734 precursor RNA, VGAM2735 precursor RNA, VGAM2736 precursor RNA, VGAM2737 precursor RNA and VGAM2738 precursor RNA, herein schematically represented by VGAM1 FOLDED PRECURSOR through VGAM3 FOLDED PRECURSOR, each of which VGAM precursor RNAs being a hairpin shaped RNA segment, corresponding to VGAM FOLDED PRECURSOR RNA of Fig. 1.

[6069] The above mentioned VGAM precursor RNAs are `diced`

by DICER COMPLEX of Fig. 1, yielding respective short RNA segments of about 22 nucleotides in length, VGAM2733 RNA, VGAM2734 RNA, VGAM2735 RNA, VGAM2736 RNA, VGAM2737 RNA and VGAM2738 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, each of which VGAM RNAs corresponding to VGAM RNA of Fig. 1.

[6070] VGAM2733 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2733 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2733 host target RNA into VGAM2733 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6071] VGAM2734 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2734 host target RNA, herein schematically

represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2734 host target RNA into VGAM2734 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6072] VGAM2735 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2735 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2735 host target RNA into VGAM2735 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6073] VGAM2736 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated re-

gion of VGAM2736 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2736 host target RNA into VGAM2736 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6074] VGAM2737 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily to a host target binding site located in an untranslated region of VGAM2737 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2737 host target RNA into VGAM2737 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6075] VGAM2738 RNA, herein schematically represented by VGAM1 RNA through VGAM3 RNA, binds complementarily

to a host target binding site located in an untranslated region of VGAM2738 host target RNA, herein schematically represented by VGAM1 HOST TARGET RNA through VGAM3 HOST TARGET RNA, which host target binding site corresponds to a host target binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III of Fig. 1, thereby inhibiting translation of VGAM2738 host target RNA into VGAM2738 host target protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN, all of Fig. 1.

[6076] It is appreciated that a function of VGR3297 gene, herein designated VGR GENE, is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGR3297 gene include diagnosis, prevention and treatment of viral infection by Broad Bean Necrosis Virus. Specific functions, and accordingly utilities, of VGR3297 gene correlate with, and may be deduced from, the identity of the host target genes, which are inhibited by VGAM RNAs comprised in the `operon-like` cluster of VGR3297 gene: VGAM2733 host target protein, VGAM2734 host target protein, VGAM2735 host target protein, VGAM2736 host target protein, VGAM2737 host target protein and VGAM2738 host target

protein, herein schematically represented by VGAM1 HOST TARGET PROTEIN through VGAM3 HOST TARGET PROTEIN. The function of these host target genes is elaborated hereinabove with reference to VGAM2733, VGAM2734, VGAM2735, VGAM2736, VGAM2737 and VGAM2738. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 15 (VGAM15) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6077] VGAM15 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM15 was detected is described hereinabove with reference to Figs. 1–8.

[6078] VGAM15 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 7. VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6079] VGAM15 gene encodes a VGAM15 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM15

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM15 precursor RNA is designated SEQ ID:1, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:1 is located at position 94429 relative to the genome of Human Herpesvirus 7.

[6080] VGAM15 precursor RNA folds onto itself, forming VGAM15 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6081] An enzyme complex designated DICER COMPLEX, `dices` the VGAM15 folded precursor RNA into VGAM15 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 77%) nucleotide sequence of VGAM15 RNA is designated SEQ ID:2726, and is provided hereinbelow with reference to the sequence listing part.

[6082] VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM15 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6083] VGAM15 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM15 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host tar-

get binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM15 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6084] The complementary binding of VGAM15 RNA, herein designated VGAM RNA, to host target binding sites on VGAM15 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM15 host target RNA into VGAM15 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6085] It is appreciated that VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM15 host target genes. The mRNA of each one of this plurality of VGAM15 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM15 RNA, herein designated VGAM RNA, and which when bound by VGAM15 RNA causes inhibition of translation of respective one or more VGAM15 host target proteins.

[6086] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM15 gene, herein designated VGAM GENE, on one or more VGAM15 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6087] It is yet further appreciated that a function of VGAM15 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM15 correlate with, and may be deduced from, the identity of the host target genes which VGAM15 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6088] Nucleotide sequences of the VGAM15 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM15 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM15 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM15 are further described hereinbelow with reference to Table 1.

[6089] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM15 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM15 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6090] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM15 gene, herein designated VGAM is inhibition of expression of VGAM15 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM15 correlate with, and may be deduced from, the identity of the target genes which VGAM15 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6091] DKFZp761D221 (Accession NM_032291) is a VGAM15 host target gene. DKFZp761D221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D221 BINDING SITE, designated SEQ ID:26056, to the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, also designated SEQ ID:2726.

[6092] A function of VGAM15 is therefore inhibition of DKFZp761D221 (Accession NM_032291). Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D221. KIAA0217 (Accession XM_040265) is another VGAM15 host target gene. KIAA0217 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0217 BINDING SITE, designated SEQ ID:33284, to the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, also designated SEQ ID:2726.

[6093] Another function of VGAM15 is therefore inhibition of KIAA0217 (Accession XM_040265). Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0217. SFRS Protein Kinase 2 (SRPK2, Accession NM_003138) is another VGAM15 host target gene. SRPK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRPK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRPK2 BINDING SITE, designated SEQ ID:9111, to the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, also designated SEQ ID:2726.

[6094] Another function of VGAM15 is therefore inhibition of

SFRS Protein Kinase 2 (SRPK2, Accession NM_003138). Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRPK2. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_012468) is another VGAM15 host target gene. TCL6 BINDING SITE1 and TCL6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 and TCL6 BINDING SITE2, designated SEQ ID:14839 and SEQ ID:21756 respectively, to the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, also designated SEQ ID:2726.

[6095] Another function of VGAM15 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_012468). Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. LOC220776 (Accession XM_043388) is another VGAM15 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33933, to the nucleotide sequence of VGAM15 RNA, herein designated VGAM RNA, also designated SEQ ID:2726.

[6096] Another function of VGAM15 is therefore inhibition of LOC220776 (Accession XM_043388). Accordingly, utilities of VGAM15 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 16 (VGAM16) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6097] VGAM16 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM16 was detected is described hereinabove with reference to Figs. 1–8.

[6098] VGAM16 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Human Herpesvirus 7. VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6099] VGAM16 gene encodes a VGAM16 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM16 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM16 precursor RNA is designated SEQ ID:2, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:2 is located at position 93652 relative to the genome of Human Herpesvirus 7.

[6100] VGAM16 precursor RNA folds onto itself, forming VGAM16 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6101] An enzyme complex designated DICER COMPLEX, `dices` the VGAM16 folded precursor RNA into VGAM16 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM16 RNA is designated SEQ ID:2727, and is provided hereinbelow with reference to the sequence listing part.

[6102] VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM16 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6103] VGAM16 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM16 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM16 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[6104] The complementary binding of VGAM16 RNA, herein designated VGAM RNA, to host target binding sites on VGAM16 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM16 host target RNA into VGAM16 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6105] It is appreciated that VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM16 host target genes. The mRNA of each one of this plurality of VGAM16 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM16 RNA, herein designated VGAM RNA, and which when bound by VGAM16 RNA causes inhibition of translation of respective one or more VGAM16 host target proteins.

[6106] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM16 gene, herein designated VGAM GENE, on one or more VGAM16 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6107] It is yet further appreciated that a function of VGAM16 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 7. Specific functions, and accordingly utilities, of VGAM16 correlate with, and may be deduced from, the identity of the host target genes which VGAM16 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6108] Nucleotide sequences of the VGAM16 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM16 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM16 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM16 are further described hereinbelow with reference to Table 1.

[6109] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM16 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM16 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6110] As mentioned hereinabove with reference to Fig. 1, a function of VGAM16 gene, herein designated VGAM is inhibition of expression of VGAM16 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM16 correlate with, and may be deduced from, the identity of the target genes which VGAM16 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6111] Protein Kinase, CGMP-dependent, Type II (PRKG2, Accession NM_006259) is a VGAM16 host target gene. PRKG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKG2 BINDING SITE, designated SEQ ID:12940, to the nucleotide sequence of VGAM16 RNA, herein designated

VGAM RNA, also designated SEQ ID:2727.

[6112] A function of VGAM16 is therefore inhibition of Protein Kinase, CGMP-dependent, Type II (PRKG2, Accession NM_006259), a gene which regulate a great variety of functions, including smooth muscle relaxation, neuronal excitability, and epithelial electrolyte transport. Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKG2. The function of PRKG2 has been established by previous studies. Nitric oxide (NO) and a broad spectrum of hormones, drugs, and toxins raise intracellular cGMP concentrations and thereby regulate a great variety of functions, including smooth muscle relaxation, neuronal excitability, and epithelial electrolyte transport. Pfeifer et al. (1996) noted that depending on the tissue, the increase in cGMP concentrations leads to the activation of different receptors, such as cyclic nucleotide phosphodiesterases. The identification of the physiologic mediator of cGMP is complicated by the existence of 2 forms of cGMP-dependent protein kinase (cGK), types I (see OMIM Ref. No. 176894) and II, which are encoded by distinct genes. Smooth muscle, platelets, and cerebellum contain high concentrations of cGK-I, whereas cGK-II is

highly concentrated in brain, lung, and intestinal mucosa. The function of cGK-II is not well understood, although there is evidence that it mediates intestinal secretion of water and electrolytes induced by the E. coli toxin STa and the intestinal peptide guanylin (OMIM Ref. No. 139392). To investigate the physiologic roles of cGK-II, Pfeifer et al. (1996) engineered a homozygous null mutation of the gene in mice by gene targeting. Mice deficient in cGK-II were resistant to E. coli STa and developed dwarfism that was caused by a severe defect in endochondral ossification at the growth plates. Membranous ossification was unaffected. Immunohistochemical staining showed a predominant expression of cGK-II in the late proliferative and early hypertrophic chondrocytes of the growth plate. Pfeifer et al. (1996) performed experiments with explanted bones from mutant and normal mice showing that the growth defect was intrinsic to the bone and not due to a general metabolic disturbance. The results indicated to the authors the central role played by cGK-II in diverse physiologic processes. Pfeifer et al. (1996) stated that identification of the pathway that mediates intestinal fluid secretion by E. coli STa has potential medical implications because STa causes traveler's diarrhea and about 50% of

infant mortality in developing countries. Orstavik et al. (1996) cloned a human cDNA encoding type II cGK by using the mouse type II cGK cDNA to probe a cerebellum cDNA library. The 762-amino acid human type II cGK protein is 96% identical to the mouse and rat type II cGK proteins. Human type II cGK is expressed as a 6-kb mRNA in prostate, small intestine, and colon and as a 4.4-kb mRNA in thymus and prostate. By PCR and Southern blotting of somatic cell hybrid panels, the authors mapped the human type II cGK gene to 4q13.1-q21.1.

[6113] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6114] Orstavik, S.; Solberg, R.; Tasken, K.; Nordahl, M.; Altherr, M. R.; Hansson, V.; Jahnsen, T.; Sandberg, M. : Molecular cloning, cDNA structure, and chromosomal localization of the human type II cGMP-dependent protein kinase. Biochem. Biophys. Res. Commun. 220: 759-765, 1996. ; and

[6115] Pfeifer, A.; Aszodi, A.; Seidler, U.; Ruth, P.; Hofmann, F.; Fassler, R. : Intestinal secretory defects and dwarfism in mice lacking cGMP-dependent protein kinase II. Science 274: 2082-.

[6116] Further studies establishing the function and utilities of PRKG2 are found in John Hopkins OMIM database record ID 601591, and in cited publications numbered 1284–1285 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp761P1010 (Accession NM_018423) is another VGAM16 host target gene. DKFZp761P1010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761P1010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761P1010 BINDING SITE, designated SEQ ID:20478, to the nucleotide sequence of VGAM16 RNA, herein designated VGAM RNA, also designated SEQ ID:2727.

[6117] Another function of VGAM16 is therefore inhibition of DKFZp761P1010 (Accession NM_018423). Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761P1010. FLJ11996 (Accession NM_024976) is another VGAM16 host target gene. FLJ11996 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11996, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11996 BINDING SITE, designated SEQ ID:24534, to the nucleotide sequence of VGAM16 RNA, herein designated VGAM RNA, also designated SEQ ID:2727.

[6118] Another function of VGAM16 is therefore inhibition of FLJ11996 (Accession NM_024976). Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11996. LOC200269 (Accession XM_114175) is another VGAM16 host target gene. LOC200269 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200269, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200269 BINDING SITE, designated SEQ ID:42761, to the nucleotide sequence of VGAM16 RNA, herein designated VGAM RNA, also designated SEQ ID:2727.

[6119] Another function of VGAM16 is therefore inhibition of LOC200269 (Accession XM_114175). Accordingly, utilities of VGAM16 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC200269. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 17 (VGAM17) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6120] VGAM17 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM17 was detected is described hereinabove with reference to Figs. 1–8.

[6121] VGAM17 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Ictalurid Herpesvirus 1. VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6122] VGAM17 gene encodes a VGAM17 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM17 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM17 precursor RNA is designated SEQ ID:3,

and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:3 is located at position 86456 relative to the genome of Ictalurid Herpesvirus 1.

[6123] VGAM17 precursor RNA folds onto itself, forming VGAM17 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6124] An enzyme complex designated DICER COMPLEX, `dices` the VGAM17 folded precursor RNA into VGAM17 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM17 RNA is designated SEQ ID:2728, and is provided hereinbelow with reference to the sequence list-

ing part.

[6125] VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM17 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6126] VGAM17 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM17 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM17 RNA, herein designated VGAM RNA, may have a different num-

ber of host target binding sites in untranslated regions of a VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6127] The complementary binding of VGAM17 RNA, herein designated VGAM RNA, to host target binding sites on VGAM17 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM17 host target RNA into VGAM17 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6128] It is appreciated that VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM17 host target genes. The mRNA of each one of this plurality of VGAM17 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM17 RNA, herein designated VGAM RNA, and which when bound by VGAM17 RNA causes in–

hibition of translation of respective one or more VGAM17 host target proteins.

[6129] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM17 gene, herein designated VGAM GENE, on one or more VGAM17 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6130] It is yet further appreciated that a function of VGAM17 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of viral infection by Ictalurid Herpesvirus 1. Specific functions, and accordingly utilities, of VGAM17 correlate with, and may be deduced from, the identity of the host target genes which VGAM17 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6131] Nucleotide sequences of the VGAM17 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM17 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM17 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM17 are further described hereinbelow with reference to Table 1.

[6132] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM17 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM17 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[6133] As mentioned hereinabove with reference to Fig. 1, a function of VGAM17 gene, herein designated VGAM is inhibition of expression of VGAM17 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM17 correlate with, and may be deduced from, the identity of the target genes which VGAM17 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6134] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974) is a VGAM17 host target gene. AKAP13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:43174, to the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, also designated SEQ ID:2728.

[6135] A function of VGAM17 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities

of VGAM17 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 has been established by previous studies. Gene map locus 15q24–q25 A–kinase anchor proteins (AKAPs; OMIM Ref. No. 602449), such as AKAP13, direct the activity of protein kinase A (PKA; OMIM Ref. No. 176911) by tethering the enzyme near its physiologic substrates. AKAP13 is also known as LBC. Catalytic GDP–GTP exchange factors (GEFs), such as LBC, play an important role in regulating the Rho/Rac GTPase cycle. The Rho/Rac family of small GTPases mediates cytoskeletal reorganization, gene transcription, and cell cycle progression through unique signal transduction pathways. By probing a breast cancer expression library using an interaction cloning strategy for proteins that bind RXR (see OMIM Ref. No. 180245), Rubino et al. (1998) obtained a full-length cDNA encoding LBC, which they called BRX (breast cancer cDNA–encoded nuclear receptor–binding auxiliary protein). The deduced 1,428–amino acid BRX protein contains a region of identity to the LBC sequence identified by Toksoz and Williams (1994) that is preceded by 3 novel regions. A fifth, C–terminal region binds the estrogen receptor (ESR1; 133430). In addition to the tis–

sues detected by Toksoz and Williams (1994), Northern blot analysis by Rubino et al. (1998) revealed BRX mRNA expression in reproductive tissues (ovary and placenta), and a 5.3-kb BRX transcript was detected in breast cancer cell lines, normal breast, and testis. Western blot and immunohistochemic analysis showed that BRX is expressed as a 170-kD protein in mammary epithelial cell lobules and terminal ducts. Binding analysis determined that BRX binds to ESR1, RXR, PPAR (OMIM Ref. No. 170998), and THR (see OMIM Ref. No. 190120). Regions 4 and 5 of BRX were shown to bind independently to the ligand-binding domain near the C terminus of ESR1 without the requirement of other bridging proteins. Overexpression of BRX in the presence of estrogen augmented the activity of an estrogen response element. ESR activation by BRX could be inhibited by a dominant-negative mutant of CDC42 (OMIM Ref. No. 116952). By genomic sequence and somatic cell hybrid analyses, Sterpetti et al. (1999) determined that proto-LBC and onco-LBC both contain N-terminal DH and PH domains; however, proto-LBC has a distinct C terminus absent in the oncoprotein. FISH with onco-LBC probes localized the LBC gene to 15q24-q25 and showed that onco-LBC represents a chimera derived from fusion with

an unrelated sequence on 7q36. Northern blot analysis detected variably sized LBC transcripts and extended the known tissue distribution to spleen and a number of cancer cell lines. Immunoblot and thin-layer chromatography analysis showed that both proto- and onco-LBC can promote the formation of GTP-bound RHOA (ARHA; 165390). Mutation analysis indicated that the transforming activity of proto-LBC is increased by truncation of the C terminus, and that the DH and PH domains, but not the chromosome 7 sequence, are required for transformation. Immunoblot analysis determined that the proto-LBC form is in the membrane fraction, while the majority of the onco-LBC product is cytosolic, indicating that the C terminus may play a major role in the subcellular localization and regulation of LBC. Using FISH with onco-LBC probes, Sterpetti et al. (1999) localized the LBC gene to 15q24-q25 and showed that onco-LBC represents a chimera derived from fusion with an unrelated sequence on 7q36.

[6136] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6137] Rubino, D.; Driggers, P.; Arbit, D.; Kemp, L.; Miller, B.; Coso, O.; Pagliai, K.; Gray, K.; Gutkind, S.; Segars, J. :

Characterization of Brx, a novel Dbl family member that modulates estrogen receptor action. *Oncogene* 16: 2513–2526, 1998. ; and

- [6138] Sterpetti, P.; Hack, A. A.; Bashar, M. P.; Park, B.; Cheng, S.-D.; Knoll, J. H. M.; Urano, T.; Feig, L. A.; Toksoz, D. : Activation of the Lbc Rho exchange factor proto-oncogene by trunc.
- [6139] Further studies establishing the function and utilities of AKAP13 are found in John Hopkins OMIM database record ID 604686, and in cited publications numbered 4378–4382 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434N014 (Accession XM_027012) is another VGAM17 host target gene. DKFZP434N014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434N014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N014 BINDING SITE, designated SEQ ID:30388, to the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, also designated SEQ ID:2728.
- [6140] Another function of VGAM17 is therefore inhibition of DK–

FZP434N014 (Accession XM_027012). Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N014. FLJ23598 (Accession NM_024783) is another VGAM17 host target gene. FLJ23598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23598 BINDING SITE, designated SEQ ID:24152, to the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, also designated SEQ ID:2728.

[6141] Another function of VGAM17 is therefore inhibition of FLJ23598 (Accession NM_024783). Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23598. LOC149086 (Accession XM_097580) is another VGAM17 host target gene. LOC149086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC149086 BINDING SITE, designated SEQ ID:40945, to the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, also designated SEQ ID:2728.

[6142] Another function of VGAM17 is therefore inhibition of LOC149086 (Accession XM_097580). Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149086. LOC92568 (Accession XM_045852) is another VGAM17 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34572, to the nucleotide sequence of VGAM17 RNA, herein designated VGAM RNA, also designated SEQ ID:2728.

[6143] Another function of VGAM17 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM17 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 18 (VGAM18) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6144] VGAM18 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM18 was detected is described hereinabove with reference to Figs. 1–8.

[6145] VGAM18 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6146] VGAM18 gene encodes a VGAM18 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM18 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM18 precursor RNA is designated SEQ ID:4, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:4 is lo-

cated at position 79665 relative to the genome of Invertebrate Iridescent Virus 6.

[6147] VGAM18 precursor RNA folds onto itself, forming VGAM18 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6148] An enzyme complex designated DICER COMPLEX, `dices` the VGAM18 folded precursor RNA into VGAM18 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM18 RNA is designated SEQ ID:2729, and is provided hereinbelow with reference to the sequence listing part.

[6149] VGAM18 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM18 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6150] VGAM18 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM18 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM18 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM18 host target RNA, herein designated VGAM

HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6151] The complementary binding of VGAM18 RNA, herein designated VGAM RNA, to host target binding sites on VGAM18 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM18 host target RNA into VGAM18 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6152] It is appreciated that VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM18 host target genes. The mRNA of each one of this plurality of VGAM18 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM18 RNA, herein designated VGAM RNA, and which when bound by VGAM18 RNA causes inhibition of translation of respective one or more VGAM18 host target proteins.

[6153] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM18 gene, herein designated VGAM GENE, on one or more VGAM18 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6154] It is yet further appreciated that a function of VGAM18 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM18 correlate with, and may be deduced from, the identity of

the host target genes which VGAM18 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6155] Nucleotide sequences of the VGAM18 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM18 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM18 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM18 are further described hereinbelow with reference to Table 1.

[6156] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM18 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM18 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6157] As mentioned hereinabove with reference to Fig. 1, a function of VGAM18 gene, herein designated VGAM is inhibition of expression of VGAM18 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM18 correlate with, and may be deduced from, the identity of the target genes which VGAM18 binds and in-

hibits, and the function of these target genes, as elaborated hereinbelow.

[6158] A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM_007203) is a VGAM18 host target gene. AKAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP2 BINDING SITE, designated SEQ ID:14063, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6159] A function of VGAM18 is therefore inhibition of A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM_007203), a gene which binds to regulatory subunit (rii) of protein kinase a. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP2. The function of AKAP2 has been established by previous studies. Gene map locus Chr.9 Protein kinase A (PKA; OMIM Ref. No. 176911) mediates actions of hormones and neurotransmitters that activate adenylate cyclase (see OMIM Ref. No. 103070). Signals carried by cAMP are often directed at discrete in-

tracellular sites. A nonuniform distribution of PKA type II molecules occurs when they are attached to the cytoskeleton by 'A-kinase anchor proteins' (see OMIM Ref. No. AKAP1, 602449). Such anchored molecules may be essential for dissemination of cAMP signals in highly polarized epithelium such as lung and kidney. Using yeast 2-hybrid screening, Dong et al. (1998) isolated cDNAs encoding 6 isoforms of a full-length 885-kD mouse protein which they termed AKAP-KL because of its expression in epithelial cells of kidney and lung. Sequence analysis showed that the isoforms are generated by alternative splicing and by utilization of either of 2 translation start codons. Using affinity chromatography and Western blot analysis, the authors showed that AKAP-KL binds PKA type II in intact cells. By immunoblot analysis of tissue fractions, Dong et al. (1998) found that AKAP-KL is abundantly expressed in lung, moderately expressed in thymus and cerebellum, but absent in heart, cerebral cortex, and liver. Confocal immunofluorescence microscopy revealed that AKAP-KL accumulates in regions of the cortical cytoskeleton in association with F-actin (see OMIM Ref. No. 102610) in human embryonic kidney cells. By radiation hybrid analysis, Nagase et al. (1999) mapped the human

AKAP gene, which they called KIAA0920, to chromosome 9.

[6160] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6161] Dong, F.; Feldmesser, M.; Casadevall, A.; Rubin, C. S. : Molecular characterization of a cDNA that encodes six isoforms of a novel murine A kinase anchor protein. J. Biol. Chem. 273: 6533–6541, 1998. ; and

[6162] Nagase, T.; Ishikawa, K.; Suyama, M.; Kikuno, R.; Hiro-sawa, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human ge.

[6163] Further studies establishing the function and utilities of AKAP2 are found in John Hopkins OMIM database record ID 604582, and in cited publications numbered 494 and 8593 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cysteine-rich Motor Neuron 1 (CRIM1, Accession NM_016441) is another VGAM18 host target gene. CRIM1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CRIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRIM1 BINDING SITE, designated SEQ ID:18561, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6164] Another function of VGAM18 is therefore inhibition of Cysteine-rich Motor Neuron 1 (CRIM1, Accession NM_016441). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRIM1. Cytochrome P450, Subfamily XXVIIIB (25-hydroxyvitamin D-1-alpha-hydroxylase), Polypeptide 1 (CYP27B1, Accession NM_000785) is another VGAM18 host target gene. CYP27B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP27B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP27B1 BINDING SITE, designated SEQ ID:6433, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6165] Another function of VGAM18 is therefore inhibition of Cy-

tochrome P450, Subfamily XXVIIIB (25-hydroxyvitamin D-1-alpha-hydroxylase), Polypeptide 1 (CYP27B1, Accession NM_000785). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP27B1. Inducible T-cell Co-stimulator (ICOS, Accession NM_012092) is another VGAM18 host target gene. ICOS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ICOS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ICOS BINDING SITE, designated SEQ ID:14383, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6166] Another function of VGAM18 is therefore inhibition of Inducible T-cell Co-stimulator (ICOS, Accession NM_012092), a gene which forms homodimers and functions as an inducible T-cell co-stimulator. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ICOS. The function of ICOS has been established by previous studies. The T cell-specific cell surface receptors

CD28 (OMIM Ref. No. 186760) and CTLA4 (OMIM Ref. No. 123890) are important regulators of the immune system. CD28 potently enhances those T-cell functions essential for an effective antigen-specific immune response, and CTLA4 counterbalances the CD28-mediated signals and thus prevents an otherwise fatal overstimulation of the lymphoid system. By generating monoclonal antibodies against activated human T cells, Hutloff et al. (1999) identified another member of this family of molecules, 'inducible costimulator,' symbolized ICOS. The ICOS-specific monoclonal antibody did not react with resting human peripheral blood T cells, but stained CD4⁺ and CD8⁺ T lymphocytes that had been activated by stimulation of the T-cell antigen receptor complex. Immunoprecipitations defined the ICOS antigen as a disulfide-linked dimer with an apparent relative molecular mass of 55 to 60 kD. Protein purification by SDS-PAGE indicated that ICOS is expressed on the cell surface as a homodimeric protein, with the 2 chains differing only in their posttranslational modification. The full-length ICOS cDNA of 2,641 basepairs was cloned from a MOLT-4V T lymphoblast cDNA library. Northern analysis revealed a single ICOS mRNA species of approximately 2.8 kb in activated human T cells. The

open reading frame of ICOS mRNA encodes a protein of 199 amino acids. The ICOS amino acid sequence shares 24% and 17% identity, respectively, with CD28 and CTLA4. The predicted mature ICOS is a type I transmembrane molecule that consists of a single immunoglobulin V-like domain, stabilized by conserved cysteine residues at positions 42 and 109; a transmembrane region of approximately 23 amino acids; and a cytoplasmic tail of 35 amino acids. It shows close structural resemblance to CD28 and CTLA4. The cysteine residue located at position 141 of CD28, also found in CTLA4, is apparently involved in forming the disulfide bridge between the homodimeric chains of these proteins, and is also found in ICOS at position 136. ICOS matches CD28 in potency and enhances all basic T-cell responses to a foreign antigen, namely proliferation, secretion of lymphokines, upregulation of molecules that mediate cell-cell interaction, and effective help for antibody secretion by B cells. Unlike the constitutively expressed CD28, ICOS has to be de novo induced on the T-cell surface and does not upregulate the production of interleukin-2 (IL2; 147680), but superinduces the synthesis of interleukin-10 (IL10; 124092), a B-cell differentiation factor. In vivo, ICOS is highly expressed on tonsillar

T cells, which are closely associated with B cells in the apical light zone of germinal centers, the site of terminal B-cell maturation. Yoshinaga et al. (1999) cloned the mouse homolog of ICOS, which they called Crp1 for 'CD28-related protein-1.' Crp1 shares 69% amino acid identity with ICOS. The sequence of ICOS, also known as 'activation-inducible lymphocyte immunomediatory molecule,' or AILIM, has been deposited in GenBank (AB023135). Coyle et al. (2000) showed that ICOS, rather than CD28, plays an important role in the production of both type 1 and type 2 cytokines by recently activated T cells. Akbari et al. (2002) noted that Th1 cells secreting IFNG (OMIM Ref. No. 147570) regulate Th2 cells and may be involved in downregulating Th2-driven airway hyperactivity and asthma. However, IFNG may also contribute to the severity of disease by exacerbating pulmonary inflammation. After exposure of mice to allergen by the respiratory route, regulatory CD4⁺ T cells (Tr) developed, producing high levels of IL10, typically considered a Th2 cytokine. The Tr cells downmodulated allergen-induced airway hyperactivity in previously sensitized mice. Both development and function of the Tr depend on the presence of IL10 and interaction with ICOS expressed on dendritic

cells. These dendritic cells also express B7-1 (CD80; 112203) and B7-2 (CD86; 601020). Akbari et al. (2002) suggested that IL10 may initially be involved in the polarization of Th2 responses but plays a regulatory role late in immune responses to attenuate Th2-driven inflammatory activity. Animal model experiments lend further support to the function of ICOS. Tafuri et al. (2001) found that reduced T-cell proliferation in cells from Icos-deficient mice was associated with a marked decrease in expression of CD40LG (OMIM Ref. No. 300386), CD25 (IL2RA; 147730), and CD69 (OMIM Ref. No. 107273). B-cell activation and T cell-independent antibody responses were unimpaired in Icos knockout mice. In contrast to the findings of McAdam et al. (2001), Tafuri et al. (2001) found that only basal levels of IgG1 were significantly reduced in Icos $-/-$ mice; however, they concurred that serum IgG1 and IgG2a levels were reduced, and IgE levels were undetectable after immunization. ELISA assays showed that this class-switching impairment was associated with reduced IL4 production but not with IFNG production. Immunohistochemistry analysis determined that germinal center formation was also reduced in Icos knockout mice, as it is in mice deficient in Cd40lg or Cd28

[6167] It is appreciated that the abovementioned animal model for ICOS is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6168] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6169] Haimila, K. E.; Partanen, J. A.; Holopainen, P. M. : Genetic polymorphism of the human ICOS gene. Immunogenetics 53: 1028–1032, 2002. ; and

[6170] Tafuri, A.; Shahinian, A.; Bladt, F.; Yoshinaga, S. K.; Jordana, M.; Wakeham, A.; Boucher, L.-M.; Bouchard, D.; Chan, V. S. F.; Duncan, G.; Odermatt, B.; Ho, A.; Itie, A.; Horan, T.; Wh.

[6171] Further studies establishing the function and utilities of ICOS are found in John Hopkins OMIM database record ID 604558, and in cited publications numbered 3683, 7380–738 and 2871–2872 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myotubularin Related Protein 2 (MTMR2, Accession NM_016156) is another VGAM18 host target gene. MTMR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MTMR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTMR2 BINDING SITE, designated SEQ ID:18243, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6172] Another function of VGAM18 is therefore inhibition of Myotubularin Related Protein 2 (MTMR2, Accession NM_016156). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTMR2. Myeloid Differentiation Primary Response Gene (88) (MYD88, Accession NM_002468) is another VGAM18 host target gene. MYD88 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYD88, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYD88 BINDING SITE, designated SEQ ID:8296, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6173] Another function of VGAM18 is therefore inhibition of

Myeloid Differentiation Primary Response Gene (88)

(MYD88, Accession NM_002468), a gene which is involved in the toll-like receptor and il-1 receptor signaling pathway in the innate immune response. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYD88.

The function of MYD88 has been established by previous studies. The myeloid differentiation (MyD) marker MyD88 was first characterized during a study of the early genetic responses of murine myeloid cells to various differentiation and growth inhibitory stimuli (Lord et al., 1990).

Myeloid differentiation primary response genes are activated in M1 myeloleukemic cells in response to interleukin-6 (IL6; 147620), which induces both growth arrest and terminal differentiation. Hardiman et al. (1997) described the cloning and gene structure of the mouse MyD88 gene. The complete coding sequence spans 5 exons, with the first exon encoding a complete 'death domain' similar to the intracellular segment of TNF receptor-1 (OMIM Ref. No. 191190). Zoo blot analysis demonstrated that it is an evolutionarily conserved gene. Northern blot analysis revealed widespread expression of the gene in many adult mouse tissues, and RT-PCR detected

MyD88 mRNA in T- and B-cell lines and differentiating embryonic stem cells. The broad expression pattern demonstrated that mouse Myd88 expression is not restricted to cells of myeloid lineage as was originally believed. Animal model experiments lend further support to the function of MYD88. Adachi et al. (1998) observed that mice with a targeted disruption of the Myd88 gene were unable to respond to IL1 (e.g., 147760), as determined by defective T-cell proliferation and the production of cytokines. Likewise, Myd88-deficient mice were unable to produce gamma-interferon (IFNG; 147570) and mediate natural killer cell activity in response to IL18 (OMIM Ref. No. 600953). NFkB activation in response to IL1 or IL18 was also impaired. These results indicated that MYD88 is a critical component in the IL1R and IL18R (OMIM Ref. No. 604494) signaling cascades. Kawai et al. (1999) extended these studies to show that responses to lipopolysaccharide, mediated by TLR4 and CD14 (OMIM Ref. No. 158120), were lost or delayed in Myd88-deficient mice, establishing that MYD88 is part of the TLR signaling cascade as well, acting just upstream of IRAK.

[6174] It is appreciated that the abovementioned animal model for MYD88 is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6175] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6176] Adachi, O.; Kawai, T.; Takeda, K.; Matsumoto, M.; Tsutsui, H.; Sakagami, M.; Nakanishi, K.; Akira, S. : Targeted disruption of the MyD88 gene results in loss of IL-1- and IL-18-mediated function. *Immunity* 143-150, 1998. ; and

[6177] Hardiman, G.; Jenkins, N. A.; Copeland, N. G.; Gilbert, D. J.; Garcia, D. K.; Naylor, S. L.; Kastelein, R. A.; Bazan, J. F. : Genetic structure and chromosomal mapping of MyD88. *Genomics*.

[6178] Further studies establishing the function and utilities of MYD88 are found in John Hopkins OMIM database record ID 602170, and in cited publications numbered 6349-6352, 12731-635 and 5992-5993 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198) is another VGAM18 host target gene. PDK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDK4, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK4 BINDING SITE, designated SEQ ID:46442, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6179] Another function of VGAM18 is therefore inhibition of Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK4. RB1-inducible Coiled-coil 1 (RB1CC1, Accession NM_014781) is another VGAM18 host target gene. RB1CC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RB1CC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RB1CC1 BINDING SITE, designated SEQ ID:16629, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6180] Another function of VGAM18 is therefore inhibition of RB1-inducible Coiled-coil 1 (RB1CC1, Accession

NM_014781), a gene which is likely to participate in nuclear architecture by connecting chromatin with the nuclear matrix or envelope. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RB1CC1. The function of RB1CC1 has been established by previous studies. By semiquantitative RT-PCR, Chano et al. (2002) found close correlation between expression of RB1CC1 and expression of the retinoblastoma gene (RB1; 180200) in a panel of cancer cell lines. In addition, they found that exogenous expression of RB1CC1 in 2 leukemia cell lines produced a marked increase in RB1 expression, with no detectable change in MDR1 levels. This induction was found to be due to activation of the RB1 promoter by RB1CC1. The RB1CC1 protein is a key regulator of the tumor suppressor gene RB1. It is localized in the nucleus and has been proposed to be a transcription factor because of its nuclear localization signal, leucine zipper motif, and coiled-coil structure (1,2:Chano et al., 2002, 2002). Chano et al. (2002) found that 7 of 35 (20%) primary breast cancers examined contained mutations in RB1CC1, including 9 large interstitial deletions predicted to yield markedly truncated RB1CC1 proteins. In all 7

cases, the RB1CC1 gene in the germline was wildtype; all deletions represented somatic mutations. Wildtype RB1CC1 and RB1 were absent or significantly less abundant than normal in the 7 cancers with mutations in RB1CC1, but were abundant in cancers without such mutations. In all 7 cancers, both RB1CC1 alleles were inactivated; 2 showed compound heterozygous deletions. Thus, RB1CC1 is frequently mutated in breast cancer and shows characteristics of a classic tumor suppressor gene.

[6181] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6182] Chano, T.; Ikegawa, S.; Kontani, K.; Okabe, H.; Baldini, N.; Saeki, Y. : Identification of RB1CC1, a novel human gene that can induce RB1 in various human cells. *Oncogene* 21: 1295–1298, 2002. ; and

[6183] Chano, T.; Kontani, K.; Teramoto, K.; Okabe, H.; Ikegawa, S. : Truncating mutations of RB1CC1 in human breast cancers. *Nature Genet.* 31: 285–288, 2002.

[6184] Further studies establishing the function and utilities of RB1CC1 are found in John Hopkins OMIM database record ID 606837, and in cited publications numbered 557 and 5580 listed in the bibliography section hereinbelow, which

are also hereby incorporated by reference. Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM_003053) is another VGAM18 host target gene. SLC18A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC18A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC18A1 BINDING SITE, designated SEQ ID:9016, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6185] Another function of VGAM18 is therefore inhibition of Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM_003053), a gene which is involved in the vesicular transport of biogenic amines. Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC18A1. The function of SLC18A1 has been established by previous studies. The physiologic and behavioral effects of pharmacologic agents that interfere with the transport of monoamine neurotransmitters into vesicles suggest that vesicular amine transport may con-

tribute to human neuropsychiatric disease. Biogenic amines have been implicated in a wide range of clinical disorders and physiologic states such as consciousness, motivation, organizational thought, mood, and motor control, sensory perception, and autonomic phenomena such as heart rate, vascular tone, and blood pressure. Peter et al. (1993) isolated a human cDNA for the brain vesicular amine transporter. They found that the brain synaptic vesicle amine transporter (SVAT) showed conservation with the corresponding gene in the rat in the regions that diverge extensively between rat SVAT and the rat adrenal chromaffin granule amine transporter (CGAT). Using the cloned sequences with a panel of mouse/human hybrids and in situ hybridization, Peter et al. (1993) mapped the adrenal CGAT gene (VMAT1) to 8p21.3 and the brain SVAT gene (OMIM Ref. No. 193001) to 10q25. This gene is also symbolized as SLC18A1. Roghani et al. (1996) showed that the mouse Slc18a1 gene maps to mouse chromosome 8 by linkage analysis.

[6186] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6187] Peter, D.; Finn, J. P.; Klisak, I.; Liu, Y.; Kojis, T.; Heinz-

mann, C.; Roghani, A.; Sparkes, R. S.; Edwards, R. H. :
Chromosomal localization of the human vesicular amine
transporter genes. Genomics 18: 720–723, 1993. ; and

[6188] Roghani, A.; Welch, C.; Xia, Y.-R.; Liu, Y.; Peter, D.; Finn, J.
P.; Edwards, R. H.; Lusk, A. J. : Assignment of the mouse
vesicular monoamine transporter genes, Slc18a1 and
Slc18a2, t.

[6189] Further studies establishing the function and utilities of
SLC18A1 are found in John Hopkins OMIM database
record ID 193002, and in cited publications numbered
10548–10549 listed in the bibliography section hereinbe-
low, which are also hereby incorporated by refer-
ence. Angiotensin II Receptor-like 2 (AGTRL2, Accession
NM_005162) is another VGAM18 host target gene.
AGTRL2 BINDING SITE is HOST TARGET binding site found
in the 5' untranslated region of mRNA encoded by
AGTRL2, corresponding to a HOST TARGET binding site
such as BINDING SITE I, BINDING SITE II or BINDING SITE III.
Table 2 illustrates the complementarity of the nucleotide
sequences of AGTRL2 BINDING SITE, designated SEQ
ID:11644, to the nucleotide sequence of VGAM18 RNA,
herein designated VGAM RNA, also designated SEQ
ID:2729.

[6190] Another function of VGAM18 is therefore inhibition of Angiotensin II Receptor-like 2 (AGTRL2, Accession NM_005162). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTRL2. BCL2-associated Athanogene 5 (BAG5, Accession NM_004873) is another VGAM18 host target gene. BAG5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG5 BINDING SITE, designated SEQ ID:11306, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6191] Another function of VGAM18 is therefore inhibition of BCL2-associated Athanogene 5 (BAG5, Accession NM_004873). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG5. DKFZP564I122 (Accession XM_032397) is another VGAM18 host target gene. DKFZP564I122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA en-

coded by DKFZP564I122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I122 BINDING SITE, designated SEQ ID:31645, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6192] Another function of VGAM18 is therefore inhibition of DKFZP564I122 (Accession XM_032397). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I122. FLJ20511 (Accession NM_017853) is another VGAM18 host target gene. FLJ20511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20511 BINDING SITE, designated SEQ ID:19529, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6193] Another function of VGAM18 is therefore inhibition of FLJ20511 (Accession NM_017853). Accordingly, utilities of

VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20511. FLJ20813 (Accession NM_017961) is another VGAM18 host target gene. FLJ20813 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20813 BINDING SITE, designated SEQ ID:19678, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6194] Another function of VGAM18 is therefore inhibition of FLJ20813 (Accession NM_017961). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20813. FLJ21140 (Accession NM_024776) is another VGAM18 host target gene. FLJ21140 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21140 BINDING SITE,

designated SEQ ID:24139, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6195] Another function of VGAM18 is therefore inhibition of FLJ21140 (Accession NM_024776). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21140. Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379) is another VGAM18 host target gene. KCNV1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNV1 BINDING SITE, designated SEQ ID:15709, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6196] Another function of VGAM18 is therefore inhibition of Potassium Channel, Subfamily V, Member 1 (KCNV1, Accession NM_014379). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNV1. KIAA0022

(Accession NM_014880) is another VGAM18 host target gene. KIAA0022 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0022, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0022 BINDING SITE, designated SEQ ID:17026, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6197] Another function of VGAM18 is therefore inhibition of KIAA0022 (Accession NM_014880). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0022. KIAA0161 (Accession NM_014746) is another VGAM18 host target gene. KIAA0161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0161 BINDING SITE, designated SEQ ID:16432, to the nucleotide sequence of VGAM18 RNA, herein designated

VGAM RNA, also designated SEQ ID:2729.

[6198] Another function of VGAM18 is therefore inhibition of KIAA0161 (Accession NM_014746). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0161. KIAA0410 (Accession NM_014778) is another VGAM18 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16614, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6199] Another function of VGAM18 is therefore inhibition of KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0410. KIAA1443 (Accession XM_033392) is another VGAM18 host target gene. KIAA1443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1443, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1443 BINDING SITE, designated SEQ ID:31930, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6200] Another function of VGAM18 is therefore inhibition of KIAA1443 (Accession XM_033392). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1443. KIAA1737 (Accession XM_041115) is another VGAM18 host target gene. KIAA1737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1737 BINDING SITE, designated SEQ ID:33447, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6201] Another function of VGAM18 is therefore inhibition of KIAA1737 (Accession XM_041115). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1737. Leucine Zipper and CTNNBIP1 Domain Containing (LZIC, Accession NM_032368) is another VGAM18 host target gene. LZIC BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LZIC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZIC BINDING SITE, designated SEQ ID:26156, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6202] Another function of VGAM18 is therefore inhibition of Leucine Zipper and CTNNBIP1 Domain Containing (LZIC, Accession NM_032368). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZIC. MGC2452 (Accession NM_032644) is another VGAM18 host target gene. MGC2452 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of MGC2452 BINDING SITE, designated SEQ ID:26373, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6203] Another function of VGAM18 is therefore inhibition of MGC2452 (Accession NM_032644). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. OS4 (Accession NM_005730) is another VGAM18 host target gene. OS4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OS4 BINDING SITE, designated SEQ ID:12290, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6204] Another function of VGAM18 is therefore inhibition of OS4 (Accession NM_005730). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OS4. Protocadherin 19 (PCDH19, Accession XM_033173) is another VGAM18

host target gene. PCDH19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH19 BINDING SITE, designated SEQ ID:31859, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6205] Another function of VGAM18 is therefore inhibition of Protocadherin 19 (PCDH19, Accession XM_033173). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH19. PRO0456 (Accession NM_014127) is another VGAM18 host target gene. PRO0456 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0456 BINDING SITE, designated SEQ ID:15392, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6206] Another function of VGAM18 is therefore inhibition of PRO0456 (Accession NM_014127). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0456. PRSC (Accession NM_006587) is another VGAM18 host target gene. PRSC BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRSC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRSC BINDING SITE, designated SEQ ID:13347, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6207] Another function of VGAM18 is therefore inhibition of PRSC (Accession NM_006587). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRSC. LOC148758 (Accession XM_086301) is another VGAM18 host target gene. LOC148758 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC148758, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148758 BINDING SITE, designated SEQ ID:38587, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6208] Another function of VGAM18 is therefore inhibition of LOC148758 (Accession XM_086301). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148758. LOC154007 (Accession XM_087824) is another VGAM18 host target gene. LOC154007 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154007 BINDING SITE, designated SEQ ID:39451, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6209] Another function of VGAM18 is therefore inhibition of LOC154007 (Accession XM_087824). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC154007. LOC90494 (Accession XM_032161) is another VGAM18 host target gene. LOC90494 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90494 BINDING SITE, designated SEQ ID:31575, to the nucleotide sequence of VGAM18 RNA, herein designated VGAM RNA, also designated SEQ ID:2729.

[6210] Another function of VGAM18 is therefore inhibition of LOC90494 (Accession XM_032161). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90494. LOC92379 (Accession XM_044712) is another VGAM18 host target gene. LOC92379 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92379, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92379 BINDING SITE, designated SEQ ID:34268, to the nucleotide sequence of VGAM18 RNA, herein designated

VGAM RNA, also designated SEQ ID:2729.

[6211] Another function of VGAM18 is therefore inhibition of LOC92379 (Accession XM_044712). Accordingly, utilities of VGAM18 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92379. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 19 (VGAM19) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6212] VGAM19 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM19 was detected is described hereinabove with reference to Figs. 1–8.

[6213] VGAM19 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6214] VGAM19 gene encodes a VGAM19 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM19 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM19 precursor RNA is designated SEQ ID:5, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:5 is located at position 63067 relative to the genome of Invertebrate Iridescent Virus 6.

[6215] VGAM19 precursor RNA folds onto itself, forming VGAM19 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6216] An enzyme complex designated DICER COMPLEX, `dices` the VGAM19 folded precursor RNA into VGAM19 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM19 RNA is designated SEQ ID:2730, and is provided hereinbelow with reference to the sequence listing part.

[6217] VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM19 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[6218] VGAM19 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM19 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM19 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6219] The complementary binding of VGAM19 RNA, herein designated VGAM RNA, to host target binding sites on VGAM19 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM19 host target RNA into VGAM19 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6220] It is appreciated that VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM19 host target genes. The mRNA of each one of this plurality of VGAM19 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM19 RNA, herein designated VGAM RNA, and which when bound by VGAM19 RNA causes inhibition of translation of respective one or more VGAM19 host target proteins.

[6221] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM19 gene, herein designated VGAM GENE, on one or more VGAM19 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6222] It is yet further appreciated that a function of VGAM19 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM19 correlate with, and may be deduced from, the identity of the host target genes which VGAM19 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6223] Nucleotide sequences of the VGAM19 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM19 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM19 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM19 are further described hereinbelow with reference to Table 1.

[6224] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM19 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM19 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6225] As mentioned hereinabove with reference to Fig. 1, a function of VGAM19 gene, herein designated VGAM is inhibition of expression of VGAM19 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM19 correlate with, and may be deduced from, the identity of the target genes which VGAM19 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6226] Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858) is a VGAM19 host target gene. COL19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL19A1 BINDING SITE, designated SEQ ID:7599, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6227] A function of VGAM19 is therefore inhibition of Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858), a gene which may act as a cross-bridge between fibrils and other extracellular matrix molecules. Accordingly, utilities

of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL19A1. The function of COL19A1 has been established by previous studies. The collagens are a large superfamily of genes that include a number of subgroups. One such group is composed of fibrillar associated collagens with interrupted triple helices (FACIT) and includes collagen types IX (e.g., 120210), XII (e.g., 120320), XIV (e.g., 120324), and XVI (e.g., 120326). Members of this group have common structural features, including short stretches of collagenous domains interrupted by non-collagenous regions. These, in turn, form functional units that serve to produce adhesion to the fibrils, provide a rigid arm that projects from the fibril and provide a point of interaction with other matrix components Yoshioka et al. (1992) mapped the COL19A1 gene to 6q12-q14, where the COL9A1 gene (OMIM Ref. No. 120210) has been mapped. Myers et al. (1993) mapped the COL19A1 gene to chromosome 6 by analysis of a panel of somatic cell hybrids. By FISH, Gerecke et al. (1997) mapped the COL19A1 gene to 6q12-q13. Khaleduzzaman et al. (1997) showed that the mouse Col19a1 gene is located on chromosome 1A3, where Col9a1 had also been mapped. They

suggested that COL19A1 and COL9A1, and their murine counterparts, were duplicated from the same ancestral gene of the FACIT family

[6228] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6229] Yoshioka, H.; Zhang, H.; Ramirez, F.; Mattei, M.-G.; Moradi-Ameli, M.; van der Rest, M.; Gordon, M. K. : Synteny between the loci for a novel FACIT-like collagen (D6S228E) and alpha 1(IX) collagen (COL9A1) on 6q12-q14 in humans. Genomics 13: 884-886, 1992. ; and

[6230] Yoshioka, H.; Zhang, H.; Ramirez, F.; Mattei, M.-G.; Moradi-Ameli, M.; van der Rest, M.; Gordon, M. K. : Synteny between the loci for a novel FACIT-like collagen (D6S228E) and alpha 1(IX).

[6231] Further studies establishing the function and utilities of COL19A1 are found in John Hopkins OMIM database record ID 120165, and in cited publications numbered 3565-3564 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM_000441) is another VGAM19 host target gene.

SLC26A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC26A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A4 BINDING SITE, designated SEQ ID:6026, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6232] Another function of VGAM19 is therefore inhibition of Solute Carrier Family 26, Member 4 (SLC26A4, Accession NM_000441). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A4. Cofactor Required For Sp1 Transcriptional Activation, Subunit 3, 130kDa (CRSP3, Accession XM_027112) is another VGAM19 host target gene. CRSP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRSP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRSP3 BINDING SITE, designated SEQ ID:30412, to the nucleotide sequence of VGAM19 RNA,

herein designated VGAM RNA, also designated SEQ ID:2730.

[6233] Another function of VGAM19 is therefore inhibition of Co-factor Required For Sp1 Transcriptional Activation, Subunit 3, 130kDa (CRSP3, Accession XM_027112). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRSP3. FLJ11320 (Accession NM_018389) is another VGAM19 host target gene. FLJ11320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11320 BINDING SITE, designated SEQ ID:20423, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6234] Another function of VGAM19 is therefore inhibition of FLJ11320 (Accession NM_018389). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11320. FLJ20045 (Accession NM_017638) is another VGAM19 host target gene. FLJ20045 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ20045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20045 BINDING SITE, designated SEQ ID:19144, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6235] Another function of VGAM19 is therefore inhibition of FLJ20045 (Accession NM_017638). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20045. KIAA0410 (Accession NM_014778) is another VGAM19 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16622, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6236] Another function of VGAM19 is therefore inhibition of

KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0410. poly(A) Binding Protein, Cytoplasmic 5 (PABPC5, Accession NM_080832) is another VGAM19 host target gene. PABPC5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PABPC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PABPC5 BINDING SITE, designated SEQ ID:28098, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6237] Another function of VGAM19 is therefore inhibition of poly(A) Binding Protein, Cytoplasmic 5 (PABPC5, Accession NM_080832). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PABPC5. LOC157292 (Accession XM_098740) is another VGAM19 host target gene. LOC157292 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC157292, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157292 BINDING SITE, designated SEQ ID:41774, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6238] Another function of VGAM19 is therefore inhibition of LOC157292 (Accession XM_098740). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157292. LOC202460 (Accession XM_114493) is another VGAM19 host target gene. LOC202460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202460 BINDING SITE, designated SEQ ID:42985, to the nucleotide sequence of VGAM19 RNA, herein designated VGAM RNA, also designated SEQ ID:2730.

[6239] Another function of VGAM19 is therefore inhibition of LOC202460 (Accession XM_114493). Accordingly, utilities of VGAM19 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC202460. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 20 (VGAM20) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6240] VGAM20 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM20 was detected is described hereinabove with reference to Figs. 1–8.

[6241] VGAM20 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6242] VGAM20 gene encodes a VGAM20 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM20 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM20 precursor RNA is designated SEQ ID:6,

and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:6 is located at position 44959 relative to the genome of Invertebrate Iridescent Virus 6.

[6243] VGAM20 precursor RNA folds onto itself, forming VGAM20 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6244] An enzyme complex designated DICER COMPLEX, `dices` the VGAM20 folded precursor RNA into VGAM20 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM20 RNA is designated SEQ ID:2731, and is provided hereinbelow with reference to the sequence list-

ing part.

[6245] VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM20 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6246] VGAM20 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM20 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM20 RNA, herein designated VGAM RNA, may have a different num-

ber of host target binding sites in untranslated regions of a VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6247] The complementary binding of VGAM20 RNA, herein designated VGAM RNA, to host target binding sites on VGAM20 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM20 host target RNA into VGAM20 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6248] It is appreciated that VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM20 host target genes. The mRNA of each one of this plurality of VGAM20 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM20 RNA, herein designated VGAM RNA, and which when bound by VGAM20 RNA causes in–

hibition of translation of respective one or more VGAM20 host target proteins.

- [6249] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM20 gene, herein designated VGAM GENE, on one or more VGAM20 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [6250] It is yet further appreciated that a function of VGAM20 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM20 correlate with, and may be deduced from, the identity of the host target genes which VGAM20 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6251] Nucleotide sequences of the VGAM20 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM20 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM20 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM20 are further described hereinbelow with reference to Table 1.

[6252] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM20 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM20 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6253] As mentioned hereinabove with reference to Fig. 1, a function of VGAM20 gene, herein designated VGAM is inhibition of expression of VGAM20 target genes. It is appreciated that specific functions, and accordingly utilities,

of VGAM20 correlate with, and may be deduced from, the identity of the target genes which VGAM20 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6254] Integrin, Alpha V (vitronectin receptor, alpha polypeptide, antigen CD51) (ITGAV, Accession NM_002210) is a VGAM20 host target gene. ITGAV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGAV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGAV BINDING SITE, designated SEQ ID:7974, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6255] A function of VGAM20 is therefore inhibition of Integrin, Alpha V (vitronectin receptor, alpha polypeptide, antigen CD51) (ITGAV, Accession NM_002210), a gene which is a member of the integrin family of cell-surface proteins. Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGAV. The function of ITGAV has been established by previous studies. A major surface antigen

family on human leukocytes includes complement receptor type 3 (CR3A; also called integrin alpha-M, Mac1 or Mo1), lymphocyte function-associated antigen type 1 (LFA-1; 153370), and p150,95 (Leu M5; 151510). These antigens share a common beta chain (OMIM Ref. No. 116920) of 94 kD, linked noncovalently to 1 of 3 alpha chains distinctive to each. They promote adhesion of granulocytes to each other and to endothelial cell monolayers. The apparent molecular weight of the Mo1 alpha chain is 155 to 165 kD, that of the LFA1 alpha subunit is 180 kD, and that of the Leu M5 subunit is 130 to 150 kD. Pierce et al. (1986) purified human Mo1 to homogeneity from normal granulocytes by affinity chromatography and high performance liquid chromatography (HPLC) and determined the N-terminal amino acid sequence of its alpha subunit. The obtained sequence was identical, except for 2 conservative substitutions, to that of the alpha subunit of Mac1 antigen (Springer et al., 1985). Furthermore, Pierce et al. (1986) found that the N-terminal amino acid sequence of the alpha subunit of Mo1 was homologous to the alpha subunit of IIb/IIIa, a glycoprotein that serves similar adhesive functions on platelets and is deficient or defective in Glanzmann thrombasthenia (OMIM Ref. No.

273800). Patients with a history of recurrent bacterial infections and an inherited deficiency of all 3 leukocyte membrane surface antigens are thought to have reduced or absent synthesis of the common beta subunit of the antigen family; see 116920. Inflammation plays an essential role in the initiation and progression of atherosclerosis. Simon et al. (2000) presented evidence that it also has a role in vascular repair after mechanical arterial injury (i.e., percutaneous transluminal coronary angioplasty, or PTCA). In animal models of vascular injury, leukocytes are recruited as a precursor to intimal thickening. Markers of leukocyte activation, in particular, increased expression of Mac1, which is responsible for firm leukocyte adhesion to platelets and fibrinogen on denuded vessels, predict restenosis after PTCA. To determine whether Mac1-mediated leukocyte recruitment is causally related to neointimal formation, Simon et al. (2000) subjected Mac1 knockout mice to a mechanical carotid artery dilation and complete endothelial denudation. They found that the selective absence of Mac1 impaired transplatelet leukocyte migration into the vessel wall, reducing leukocyte accumulation. Diminished medial leukocyte accumulation was accompanied by markedly reduced neointimal

thickening after vascular injury. These data established a role for inflammation in neointimal thickening and suggested that leukocyte recruitment to mechanically injured arteries may prevent restenosis

[6256] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6257] Pierce, M. W.; Remold-O'Donnell, E.; Todd, R. F., III; Arnaout, M. A. : N-terminal sequence of human leukocyte glycoprotein Mo1: conservation across species and homology to platelet IIb/IIIa. *Biochim. Biophys. Acta* 874: 368–371, 1986. ; and

[6258] Simon, D. I.; Chen, Z.; Seifert, P.; Edelman, E. R.; Ballantyne, C. M.; Rogers, C. : Decreased neointimal formation in Mac-1 $-/-$ mice reveals a role for inflammation in vascular repair a.

[6259] Further studies establishing the function and utilities of ITGAV are found in John Hopkins OMIM database record ID 193210, and in cited publications numbered 518–519, 3336, 3338–3339, 52 and 12455–12456 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Thrombospondin 1 (THBS1, Accession NM_003246) is another VGAM20 host target gene.

THBS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by THBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBS1 BINDING SITE, designated SEQ ID:9257, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6260] Another function of VGAM20 is therefore inhibition of Thrombospondin 1 (THBS1, Accession NM_003246), a gene which is a member of a family of adhesive molecules, involves in blood clotting and in angiogenesis. Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBS1. The function of THBS1 has been established by previous studies. Natural inhibitors of angiogenesis are able to block pathologic neovascularization without harming the preexisting vasculature. Volpert et al. (2002) demonstrated that 2 such inhibitors, thrombospondin I and pigment epithelium-derived factor (OMIM Ref. No. 172860), derive specificity for remodeling vessels from their dependence on Fas/Fas ligand (134637; 134638)-mediated apoptosis to block angiogenesis. Both

inhibitors upregulated FasL on endothelial cells. Expression of the essential partner of FasL, Fas receptor, was low on quiescent endothelial cells and vessels but greatly enhanced by inducers of angiogenesis, thereby specifically sensitizing the stimulated cells to apoptosis by inhibitor-generated FasL. The antiangiogenic activity of thrombospondin I and pigment epithelium-derived factor both in vitro and in vivo was dependent on this dual induction of Fas and FasL and the resulting apoptosis. Volpert et al. (2002) concluded that this example of cooperation between pro- and antiangiogenic factors in the inhibition of angiogenesis provides one explanation for the ability of inhibitors to select remodeling capillaries for destruction. Animal model experiments lend further support to the function of THBS1. To explore the function of thrombospondin I in vivo, Lawler et al. (1998) disrupted the Thbs1 gene by homologous recombination in the mouse genome. Platelets from these mice were completely deficient in Thbs1 protein; however, thrombin-induced platelet aggregation was not diminished. The deficient mice displayed a mild and variable lordotic curvature of the spine that was apparent from birth. They also displayed an increase in the number of circulating white

blood cells, with monocytes and eosinophils having the largest percent increases. Although other major organs showed no abnormalities consistent with high levels of expression of Thbs1 in lung, Lawler et al. (1998) observed abnormalities in the lungs of the mice lacking Thbs1. Extensive acute and organizing pneumonia with neutrophils and macrophages developed by 4 weeks of age. The macrophages stained for hemosiderin, indicating that diffuse alveolar hemorrhage was occurring. Later, the number of neutrophils decreased and a striking increase in the number of hemosiderin-containing macrophages was observed associated with multiple-lineage epithelial hyperplasia and the deposition of collagen and elastin. The results indicated that THBS1 is involved in normal lung homeostasis.

[6261] It is appreciated that the abovementioned animal model for THBS1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6262] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6263] Lawler, J.; Sunday, M.; Thibert, V.; Duquette, M.; George,

E. L.; Rayburn, H.; Hynes, R. O. : Thrombospondin-1 is required for normal murine pulmonary homeostasis and its absence causes pneumonia. J. Clin. Invest. 101: 982-992, 1998. ; and

[6264] Volpert, O. V.; Zaichuk, T.; Zhou, W.; Reiher, F.; Ferguson, T. A.; Stuart, P. M.; Amin, M.; Bouck, N. P. : Inducer-stimulated Fas targets activated endothelium for destruction by anti-a.

[6265] Further studies establishing the function and utilities of THBS1 are found in John Hopkins OMIM database record ID 188060, and in cited publications numbered 10515-10521, 37 and 10522 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP564O123 (Accession XM_002810) is another VGAM20 host target gene. DKFZP564O123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O123 BINDING SITE, designated SEQ ID:29905, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ

ID:2731.

[6266] Another function of VGAM20 is therefore inhibition of DKFZP564O123 (Accession XM_002810). Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O123. KIAA0336 (Accession NM_014635) is another VGAM20 host target gene. KIAA0336 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0336 BINDING SITE, designated SEQ ID:16010, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6267] Another function of VGAM20 is therefore inhibition of KIAA0336 (Accession NM_014635). Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0336. KIAA1494 (Accession XM_043561) is another VGAM20 host target gene. KIAA1494 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1494, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1494 BINDING SITE, designated SEQ ID:33961, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6268] Another function of VGAM20 is therefore inhibition of KIAA1494 (Accession XM_043561). Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1494. RYK Receptor-like Tyrosine Kinase (RYK, Accession XM_093692) is another VGAM20 host target gene. RYK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RYK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RYK BINDING SITE, designated SEQ ID:40204, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6269] Another function of VGAM20 is therefore inhibition of RYK Receptor-like Tyrosine Kinase (RYK, Accession XM_093692). Accordingly, utilities of VGAM20 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with RYK. LOC123047 (Accession XM_063456) is another VGAM20 host target gene.

LOC123047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123047 BINDING SITE, designated SEQ ID:37237, to the nucleotide sequence of VGAM20 RNA, herein designated VGAM RNA, also designated SEQ ID:2731.

[6270] Another function of VGAM20 is therefore inhibition of LOC123047 (Accession XM_063456). Accordingly, utilities of VGAM20 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123047. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 21 (VGAM21) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6271] VGAM21 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM21 was detected is described hereinabove with reference to Figs. 1–8.

[6272] VGAM21 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6273] VGAM21 gene encodes a VGAM21 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM21 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM21 precursor RNA is designated SEQ ID:7, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:7 is located at position 5472 relative to the genome of Invertebrate Iridescent Virus 6.

[6274] VGAM21 precursor RNA folds onto itself, forming VGAM21 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin struc-

ture`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6275] An enzyme complex designated DICER COMPLEX, `dices` the VGAM21 folded precursor RNA into VGAM21 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM21 RNA is designated SEQ ID:2732, and is provided hereinbelow with reference to the sequence listing part.

[6276] VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM21 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING

and 3`UTR respectively.

[6277] VGAM21 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM21 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM21 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6278] The complementary binding of VGAM21 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM21 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM21 host target RNA into VGAM21 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6279] It is appreciated that VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM21 host target genes. The mRNA of each one of this plurality of VGAM21 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM21 RNA, herein designated VGAM RNA, and which when bound by VGAM21 RNA causes inhibition of translation of respective one or more VGAM21 host target proteins.

[6280] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM21 gene, herein designated VGAM GENE, on one or more VGAM21 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known

non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6281] It is yet further appreciated that a function of VGAM21 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM21 correlate with, and may be deduced from, the identity of the host target genes which VGAM21 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6282] Nucleotide sequences of the VGAM21 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM21 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM21 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM21 are further described hereinbelow with reference to Table 1.

[6283] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM21 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM21 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6284] As mentioned hereinabove with reference to Fig. 1, a function of VGAM21 gene, herein designated VGAM is inhibition of expression of VGAM21 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM21 correlate with, and may be deduced from, the identity of the target genes which VGAM21 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6285] XT3 (Accession NM_020208) is a VGAM21 host target gene. XT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XT3, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XT3 BINDING SITE, designated SEQ ID:21443, to the nucleotide sequence of VGAM21 RNA, herein designated VGAM RNA, also designated SEQ ID:2732.

[6286] A function of VGAM21 is therefore inhibition of XT3 (Accession NM_020208), a gene which is a Kidney-specific orphan transporter. Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XT3. The function of XT3 has been established by previous studies. Na(+) and Cl(-)-coupled transporter proteins mediate transit of structurally related small hydrophilic substances across plasma membranes. These transporters are structurally related to a small subgroup of proteins with no known substrates. By screening a mouse kidney cDNA library, Nash et al. (1998) obtained cDNAs encoding 2 members of this subgroup, Xt2 and Xt3. Using mouse Xt3 to screen a human kidney cDNA library, they obtained a partial sequence encoding human XT3. Sequence analysis predicted that the mouse sequence, approximately 88% identical to human XT3 and rat B21a, contains 12 potential trans-membrane domains. Northern blot analysis detected 3.2-

and 4.0-kb XT3 transcripts in human kidney and small intestine, with no expression detected in other tissues. Expression was slightly higher in kidney, where an 8.5-kb transcript was also detected. Immunofluorescence microscopy demonstrated expression on the plasma membrane of transfected cells. Nash et al. (1998) tested numerous substrates but failed to identify a compound transported by Xt3. Nash et al. (1998) mapped the mouse Xt3 gene to chromosome 9, near the telomere. Scott (2001) mapped the human XT3 gene to chromosome 3 based on sequence similarity between the XT3 sequence (GenBank AF075260) and a chromosome 3 clone (GenBank AC005669).

[6287] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6288] Nash, S. R.; Giros, B.; Kingsmore, S. F.; Kim, K. M.; El-Mestikawy, S.; Dong, Q.; Fumagalli, F.; Seldin, M. F.; Caron, M. G. : Cloning, gene structure and genomic localization of an orphan transporter from mouse kidney with six alternatively-spliced isoforms. *Receptors Channels* 6: 113–128, 1998. ; and

[6289] Scott, A. F. : Personal Communication. Baltimore, Md.,

2/5/2001.

[6290] Further studies establishing the function and utilities of XT3 are found in John Hopkins OMIM database record ID 605616, and in cited publications numbered 6777–6778 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. COE2 (Accession XM_034639) is another VGAM21 host target gene. COE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COE2 BINDING SITE, designated SEQ ID:32131, to the nucleotide sequence of VGAM21 RNA, herein designated VGAM RNA, also designated SEQ ID:2732.

[6291] Another function of VGAM21 is therefore inhibition of COE2 (Accession XM_034639). Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COE2. POLD3 (Accession XM_166243) is another VGAM21 host target gene. POLD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLD3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLD3 BINDING SITE, designated SEQ ID:44052, to the nucleotide sequence of VGAM21 RNA, herein designated VGAM RNA, also designated SEQ ID:2732.

[6292] Another function of VGAM21 is therefore inhibition of POLD3 (Accession XM_166243). Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLD3. RI58 (Accession NM_012420) is another VGAM21 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RI58, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ ID:14794, to the nucleotide sequence of VGAM21 RNA, herein designated VGAM RNA, also designated SEQ ID:2732.

[6293] Another function of VGAM21 is therefore inhibition of RI58 (Accession NM_012420). Accordingly, utilities of VGAM21 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. Fig.

1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 22 (VGAM22) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6294] VGAM22 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM22 was detected is described hereinabove with reference to Figs. 1–8.

[6295] VGAM22 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6296] VGAM22 gene encodes a VGAM22 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM22 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM22 precursor RNA is designated SEQ ID:8, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:8 is lo-

cated at position 22721 relative to the genome of Invertebrate Iridescent Virus 6.

[6297] VGAM22 precursor RNA folds onto itself, forming VGAM22 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6298] An enzyme complex designated DICER COMPLEX, `dices` the VGAM22 folded precursor RNA into VGAM22 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM22 RNA is designated SEQ ID:2733, and is provided hereinbelow with reference to the sequence listing part.

[6299] VGAM22 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM22 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6300] VGAM22 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM22 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM22 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM22 host target RNA, herein designated VGAM

HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6301] The complementary binding of VGAM22 RNA, herein designated VGAM RNA, to host target binding sites on VGAM22 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM22 host target RNA into VGAM22 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6302] It is appreciated that VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM22 host target genes. The mRNA of each one of this plurality of VGAM22 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM22 RNA, herein designated VGAM RNA, and which when bound by VGAM22 RNA causes inhibition of translation of respective one or more VGAM22 host target proteins.

[6303] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM22 gene, herein designated VGAM GENE, on one or more VGAM22 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6304] It is yet further appreciated that a function of VGAM22 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM22 correlate with, and may be deduced from, the identity of

the host target genes which VGAM22 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6305] Nucleotide sequences of the VGAM22 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM22 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM22 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM22 are further described hereinbelow with reference to Table 1.

[6306] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM22 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM22 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6307] As mentioned hereinabove with reference to Fig. 1, a function of VGAM22 gene, herein designated VGAM is inhibition of expression of VGAM22 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM22 correlate with, and may be deduced from, the identity of the target genes which VGAM22 binds and in-

hibits, and the function of these target genes, as elaborated hereinbelow.

[6308] Adenylate Cyclase 6 (ADCY6, Accession NM_015270) is a VGAM22 host target gene. ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADCY6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2, designated SEQ ID:17589 and SEQ ID:21977 respectively, to the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, also designated SEQ ID:2733.

[6309] A function of VGAM22 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM_015270), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY6. The function of ADCY6 has been established by previous studies. By Southern blot analysis of somatic cell hybrid DNAs, Gaudin et al. (1994) mapped the ADCY6 gene to chromo-

some 12. Using isotopic in situ hybridization, Haber et al. (1994) mapped the ADCY6 gene to 12q12–q13. By fluorescence in situ hybridization, Edelhoff et al. (1995) confirmed the assignment of ADCY6 to 12q13 and demonstrated that the homologous mouse gene is located on chromosome 15 in the F region.

[6310] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6311] Edelhoff, S.; Villacres, E. C.; Storm, D. R.; Disteché, C. M. : Mapping of adenylyl cyclase genes type I, II, III, IV, V, and VI in mouse. *Mammalian Genome* 6: 111–113, 1995. ; and

[6312] Gaudin, C.; Homcy, C. J.; Ishikawa, Y. : Mammalian adenylyl cyclase family members are randomly located on different chromosomes. *Hum. Genet.* 94: 527–529, 1994.

[6313] Further studies establishing the function and utilities of ADCY6 are found in John Hopkins OMIM database record ID 600294, and in cited publications numbered 494–49 and 10136 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MORF (Accession NM_012330) is another VGAM22 host target gene. MORF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

MORF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MORF BINDING SITE, designated SEQ ID:14720, to the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, also designated SEQ ID:2733.

[6314] Another function of VGAM22 is therefore inhibition of MORF (Accession NM_012330). Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MORF. FLJ13111 (Accession NM_025082) is another VGAM22 host target gene. FLJ13111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13111, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13111 BINDING SITE, designated SEQ ID:24685, to the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, also designated SEQ ID:2733.

[6315] Another function of VGAM22 is therefore inhibition of FLJ13111 (Accession NM_025082). Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ13111. KIAA0495 (Accession XM_031397) is another VGAM22 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31366, to the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, also designated SEQ ID:2733.

[6316] Another function of VGAM22 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. LOC145988 (Accession XM_085290) is another VGAM22 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38034, to

the nucleotide sequence of VGAM22 RNA, herein designated VGAM RNA, also designated SEQ ID:2733.

[6317] Another function of VGAM22 is therefore inhibition of LOC145988 (Accession XM_085290). Accordingly, utilities of VGAM22 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 23 (VGAM23) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6318] VGAM23 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM23 was detected is described hereinabove with reference to Figs. 1–8.

[6319] VGAM23 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6320] VGAM23 gene encodes a VGAM23 precursor RNA, herein

designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM23 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM23 precursor RNA is designated SEQ ID:9, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:9 is located at position 56871 relative to the genome of Invertebrate Iridescent Virus 6.

[6321] VGAM23 precursor RNA folds onto itself, forming VGAM23 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6322] An enzyme complex designated DICER COMPLEX, `dices` the VGAM23 folded precursor RNA into VGAM23 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM23 RNA is designated SEQ ID:2734, and is provided hereinbelow with reference to the sequence listing part.

[6323] VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM23 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[6324] VGAM23 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM23 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, desig-

nated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM23 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6325] The complementary binding of VGAM23 RNA, herein designated VGAM RNA, to host target binding sites on VGAM23 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM23 host target RNA into VGAM23 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6326] It is appreciated that VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM23 host target genes. The mRNA of

each one of this plurality of VGAM23 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM23 RNA, herein designated VGAM RNA, and which when bound by VGAM23 RNA causes inhibition of translation of respective one or more VGAM23 host target proteins.

[6327] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM23 gene, herein designated VGAM GENE, on one or more VGAM23 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6328] It is yet further appreciated that a function of VGAM23 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM23 correlate with, and may be deduced from, the identity of the host target genes which VGAM23 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6329] Nucleotide sequences of the VGAM23 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM23 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM23 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM23 are further described hereinbelow with reference to Table 1.

[6330] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM23 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM23 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[6331] As mentioned hereinabove with reference to Fig. 1, a function of VGAM23 gene, herein designated VGAM is inhibition of expression of VGAM23 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM23 correlate with, and may be deduced from, the identity of the target genes which VGAM23 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6332] Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM_001399) is a VGAM23 host target gene. ED1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ED1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ED1 BINDING SITE, designated SEQ ID:7099, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6333] A function of VGAM23 is therefore inhibition of Ectodermal Dysplasia 1, Anhidrotic (ED1, Accession NM_001399). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with ED1. Ephrin-B2 (EFNB2, Accession NM_004093) is another VGAM23 host target gene. EFNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB2 BINDING SITE, designated SEQ ID:10296, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6334] Another function of VGAM23 is therefore inhibition of Ephrin-B2 (EFNB2, Accession NM_004093). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNB2. Protocadherin Gamma Subfamily A, 1 (PCDHGA1, Accession NM_018912) is another VGAM23 host target gene. PCDHGA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA1 BINDING SITE, designated SEQ ID:20981, to the nucleotide sequence of

VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6335] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 1 (PCDHGA1, Accession NM_018912). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA1. Protocadherin Gamma Subfamily A, 10 (PCDHGA10, Accession NM_018913) is another VGAM23 host target gene. PCDHGA10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA10 BINDING SITE, designated SEQ ID:20982, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6336] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 10 (PCDHGA10, Accession NM_018913). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA10. Protocad-

herin Gamma Subfamily A, 11 (PCDHGA11, Accession NM_018914) is another VGAM23 host target gene. PCDHGA11 BINDING SITE1 and PCDHGA11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHGA11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA11 BINDING SITE1 and PCDHGA11 BINDING SITE2, designated SEQ ID:20984 and SEQ ID:25790 respectively, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6337] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 11 (PCDHGA11, Accession NM_018914). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA11. Protocadherin Gamma Subfamily A, 2 (PCDHGA2, Accession NM_018915) is another VGAM23 host target gene. PCDHGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PCDHGA2 BINDING SITE, designated SEQ ID:20985, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6338] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 2 (PCDHGA2, Accession NM_018915). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA2. Protocadherin Gamma Subfamily A, 3 (PCDHGA3, Accession NM_018916) is another VGAM23 host target gene. PCDHGA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA3 BINDING SITE, designated SEQ ID:20986, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6339] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 3 (PCDHGA3, Acces-

sion NM_018916), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA3. The function of PCDHGA3 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGA3 is a member of subfamily A of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. Using PCR on a brain cDNA library, Wu and Maniatis (1999) obtained cDNAs encoding 2 isoforms of PCDHGA3. Sequence analysis predicted that the long isoform of PCDHGA3 contains 932 amino acids (GenBank AAD43717) and is 48% identical to PCDHGC4 (OMIM Ref. No. 606305). The C-terminal 134 amino acids of PCDHGA3 and PCDHGC4 are identical and have a lysine-rich motif. PCDHGA3 has a signal peptide, 4 putative N-linked glycosylation sites, and 6 cadherin ectodomains.

[6340] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6341] Wu, Q.; Maniatis, T. : A striking organization of a large family of human neural cadherin like cell adhesion genes. Cell 97: 779–790, 1999. ; and

[6342] Wu, Q.; Zhang, T.; Cheng, J.–F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse a.

[6343] Further studies establishing the function and utilities of PCDHGA3 are found in John Hopkins OMIM database record ID 606290, and in cited publications numbered 675 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Gamma Subfamily A, 4 (PCDHGA4, Accession NM_018917) is another VGAM23 host target gene. PCDHGA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA4 BINDING SITE, designated SEQ ID:20987, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6344] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 4 (PCDHGA4, Accession NM_018917). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA4. Protocadherin Gamma Subfamily A, 5 (PCDHGA5, Accession NM_018918) is another VGAM23 host target gene. PCDHGA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA5 BINDING SITE, designated SEQ ID:20988, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6345] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 5 (PCDHGA5, Accession NM_018918), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA5. The function of PCDHGA5 has been established by previ-

ous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGA5 is a member of subfamily A of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. Using PCR with degenerate primers to screen melanoma cell lines, Matsuyoshi et al. (1997) obtained a cDNA fragment encoding part of PCDHGA5, which they termed ME3. RT-PCR analysis detected expression of ME3 in 1 of 2 melanoma cell lines but not in normal melanocytes.

[6346] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6347] Matsuyoshi, N.; Tanaka, T.; Toda, K.; Imamura, S. : Identification of novel cadherins expressed in human melanoma cells. *J. Invest. Derm.* 108: 908-913, 1997. ; and

[6348] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse an.

[6349] Further studies establishing the function and utilities of PCDHGA5 are found in John Hopkins OMIM database

record ID 606292, and in cited publications numbered 451 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Gamma Subfamily A, 6 (PCDHGA6, Accession NM_018919) is another VGAM23 host target gene. PCDHGA6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA6 BINDING SITE, designated SEQ ID:20989, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6350] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 6 (PCDHGA6, Accession NM_018919). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA6. Protocadherin Gamma Subfamily A, 7 (PCDHGA7, Accession NM_018920) is another VGAM23 host target gene. PCDHGA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCD-

HGA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA7 BINDING SITE, designated SEQ ID:20990, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6351] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 7 (PCDHGA7, Accession NM_018920). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA7. Protocadherin Gamma Subfamily A, 8 (PCDHGA8, Accession NM_032088) is another VGAM23 host target gene. PCDHGA8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA8 BINDING SITE, designated SEQ ID:25787, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6352] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 8 (PCDHGA8, Accession NM_032088), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA8. The function of PCDHGA8 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGA8 is a member of subfamily A of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. By screening a brain cDNA library for genes with the potential to encode large proteins, Nagase et al. (1997) identified a cDNA encoding PCDHGA8, which they termed KIAA0327. The 820-amino acid protein was predicted to be involved in cell signaling. RT-PCR analysis detected weak expression in placenta and kidney.

[6353] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6354] Nagase, T.; Ishikawa, K.; Nakajima, D.; Ohira, M.; Seki, N.;

Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 4: 141–150, 1997. ; and

[6355] Wu, Q.; Zhang, T.; Cheng, J.–F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse an.

[6356] Further studies establishing the function and utilities of PCDHGA8 are found in John Hopkins OMIM database record ID 606295, and in cited publications numbered 95 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Gamma Subfamily A, 9 (PCDHGA9, Accession NM_018921) is another VGAM23 host target gene. PCDHGA9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDHGA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA9 BINDING SITE, designated SEQ ID:20991, to the nucleotide sequence of VGAM23 RNA,

herein designated VGAM RNA, also designated SEQ ID:2734.

[6357] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily A, 9 (PCDHGA9, Accession NM_018921). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA9. Protocadherin Gamma Subfamily B, 1 (PCDHGB1, Accession NM_018922) is another VGAM23 host target gene. PCDHGB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB1 BINDING SITE, designated SEQ ID:20992, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6358] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 1 (PCDHGB1, Accession NM_018922). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB1. Protocad-

herin Gamma Subfamily B, 2 (PCDHGB2, Accession NM_018923) is another VGAM23 host target gene. PCDHGB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB2 BINDING SITE, designated SEQ ID:20993, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6359] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 2 (PCDHGB2, Accession NM_018923). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB2. Protocadherin Gamma Subfamily B, 3 (PCDHGB3, Accession NM_018924) is another VGAM23 host target gene. PCDHGB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of PCDHGB3 BINDING SITE, designated SEQ ID:20994, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6360] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 3 (PCDHGB3, Accession NM_018924). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB3. Protocadherin Gamma Subfamily B, 4 (PCDHGB4, Accession NM_003736) is another VGAM23 host target gene. PCDHGB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB4 BINDING SITE, designated SEQ ID:9827, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6361] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 4 (PCDHGB4, Accession NM_003736), a gene which is a potential calcium-

dependent cell–adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB4. The function of PCDHGB4 has been established by previous studies. Cadherins are calcium–dependent cell–cell adhesion molecules that mediate neural cell–cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGB4 is a member of subfamily B of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. To elucidate the molecular basis of fibroblast cell–cell adhesion, Matsuyoshi and Imamura (1997) investigated cadherin expression in human fibroblasts by RT–PCR using degenerate primers based on well–conserved amino acid sequences of cadherins. They isolated a partial cDNA encoding PCDHGB4, which they called FIB2. RT–PCR analysis revealed that FIB2 is expressed in fibroblasts but not in melanocytes or keratinocytes.

[6362] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6363] Matsuyoshi, N.; Imamura, S. : Multiple cadherins are expressed in human fibroblasts. *Biochem. Biophys. Res.*

Commun. 235: 355–358, 1997. ; and

[6364] Wu, Q.; Zhang, T.; Cheng, J.–F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse an.

[6365] Further studies establishing the function and utilities of PCDHGB4 are found in John Hopkins OMIM database record ID 603058, and in cited publications numbered 848 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Gamma Subfamily B, 5 (PCDHGB5, Accession NM_018925) is another VGAM23 host target gene. PCDHGB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB5 BINDING SITE, designated SEQ ID:20995, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6366] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 5 (PCDHGB5, Acces–

sion NM_018925). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB5. Protocadherin Gamma Subfamily B, 6 (PCDHGB6, Accession NM_018926) is another VGAM23 host target gene. PCDHGB6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGB6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB6 BINDING SITE, designated SEQ ID:20996, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6367] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 6 (PCDHGB6, Accession NM_018926). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB6. Protocadherin Gamma Subfamily B, 7 (PCDHGB7, Accession NM_018927) is another VGAM23 host target gene. PCDHGB7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCD-

HGB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGB7 BINDING SITE, designated SEQ ID:20997, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6368] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily B, 7 (PCDHGB7, Accession NM_018927), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGB7. The function of PCDHGB7 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGB7 is a member of subfamily B of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. Using PCR with degenerate primers to screen melanoma cell lines, Matsuyoshi et al. (1997) obtained a cDNA fragment encoding part of PCDHGB7, which they termed ME6. RT-

PCR analysis detected expression of ME6 in 2 melanoma cell lines, a squamous cell carcinoma cell line, and normal fibroblasts and melanocytes.

[6369] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6370] Matsuyoshi, N.; Tanaka, T.; Toda, K.; Imamura, S. : Identification of novel cadherins expressed in human melanoma cells. J. Invest. Derm. 108: 908–913, 1997. ; and

[6371] Wu, Q.; Zhang, T.; Cheng, J.–F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse an.

[6372] Further studies establishing the function and utilities of PCDHGB7 are found in John Hopkins OMIM database record ID 606304, and in cited publications numbered 451 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Gamma Subfamily C, 3 (PCDHGC3, Accession NM_032403) is another VGAM23 host target gene. PCDHGC3 BINDING SITE1 and PCDHGC3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHGC3, corresponding to

HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGC3 BINDING SITE1 and PCDHGC3 BINDING SITE2, designated SEQ ID:26188 and SEQ ID:8450 respectively, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6373] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily C, 3 (PCDHGC3, Accession NM_032403), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGC3. The function of PCDHGC3 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHGC3 is a member of subfamily C of the gamma cluster of protocadherin genes on 5q31. For specific information on the PCDHG genes, see 604968. Sano et al. (1993) isolated cDNAs encoding PCDHGC3, which they termed pc43, and other protocadherins from several organisms. Like pc42 (OMIM Ref. No. 603626), human

pc43 contains an N-terminal extracellular domain, a transmembrane domain, and a C-terminal cytoplasmic region. On Western blots of extracts of a human neuroblastoma cell line, pc43 migrated at 150 kD. Immunofluorescence microscopy localized pc43 to the periphery of cells, primarily in cell-cell contact sites. Cells expressing pc43 showed cell aggregation activity.

[6374] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6375] Sano, K.; Tanihara, H.; Heimark, R. L.; Obata, S.; Davidson, M.; St. John, T.; Taketani, S.; Suzuki, S. : Protocadherins: a large family of cadherin-related molecules in central nervous system. EMBO J. 12: 2249-2256, 1993. ; and

[6376] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse and.

[6377] Further studies establishing the function and utilities of PCDHGC3 are found in John Hopkins OMIM database record ID 603627, and in cited publications numbered 6861, 762 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Protocadherin Gamma Subfamily C, 5 (PCDHGC5, Accession NM_018929) is another VGAM23 host target gene. PCDHGC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHGC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGC5 BINDING SITE, designated SEQ ID:20999, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6378] Another function of VGAM23 is therefore inhibition of Protocadherin Gamma Subfamily C, 5 (PCDHGC5, Accession NM_018929). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGC5. Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283) is another VGAM23 host target gene. TACC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TACC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TACC1 BINDING SITE, designated SEQ ID:12963, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6379] Another function of VGAM23 is therefore inhibition of Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACC1. TEM7 (Accession NM_020405) is another VGAM23 host target gene. TEM7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM7 BINDING SITE, designated SEQ ID:21674, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6380] Another function of VGAM23 is therefore inhibition of TEM7 (Accession NM_020405), a gene which involves in angiogenesis. Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with TEM7. The function of TEM7 has been established by previous studies. Using serial analysis of gene expression (SAGE), St Croix et al. (2000) identified partial cDNAs corresponding to several tumor endothelial markers (TEMs) that displayed elevated expression during tumor angiogenesis. Among the genes they identified was TEM7. Using database searches and 5-prime RACE, Carson-Walter et al. (2001) derived sequences covering the entire TEM7 coding region, which encodes a 500-amino acid type I transmembrane protein containing a plexin-like domain. An alternate transcript of the TEM7 gene had been designated TEM3 by St Croix et al. (2000). TEM3 and TEM7 differ in the use of alternative polyadenylation sites but result in the same predicted protein. The mouse ortholog of TEM7 shares 81% amino acid identity with the human protein. In situ hybridization analysis of human colorectal cancer by Carson-Walter et al. (2001) demonstrated that TEM7 was expressed clearly in the endothelial cells of the tumor stroma but not in the endothelial cells of normal colonic tissue. Using in situ hybridization to assay expression in various normal adult mouse tissues, they observed that Tem7 was largely undetectable in mouse tissues or tumors, but was abun-

dantly expressed in mouse brain. Carson-Walter et al. (2001) localized Tem7 expression to Purkinje cells of the cerebellum and some neuronal cells.

[6381] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6382] Carson-Walter, E. B.; Watkins, D. N.; Nanda, A.; Vogelstein, B.; Kinzler, K. W.; St. Croix, B. : Cell surface tumor endothelial markers are conserved in mice and humans. Cancer Res. 61: 6649-6655, 2001. ; and

[6383] St. Croix, B.; Rago, C.; Velculescu, V.; Traverso, G.; Romans, K. E.; Montgomery, E.; Lal, A.; Riggins, G. J.; Lengauer, C.; Vogelstein, B.; Kinzler, K. W. : Genes expressed in human tu.

[6384] Further studies establishing the function and utilities of TEM7 are found in John Hopkins OMIM database record ID 606826, and in cited publications numbered 689 and 6907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Eukaryotic Translation Initiation Factor 4B (EIF4B, Accession XM_071605) is another VGAM23 host target gene. EIF4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF4B, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF4B BINDING SITE, designated SEQ ID:37402, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6385] Another function of VGAM23 is therefore inhibition of Eukaryotic Translation Initiation Factor 4B (EIF4B, Accession XM_071605). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF4B. FLJ13150 (Accession NM_024813) is another VGAM23 host target gene. FLJ13150 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13150 BINDING SITE, designated SEQ ID:24201, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6386] Another function of VGAM23 is therefore inhibition of FLJ13150 (Accession NM_024813). Accordingly, utilities of

VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13150. FLJ14327 (Accession NM_024912) is another VGAM23 host target gene. FLJ14327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14327 BINDING SITE, designated SEQ ID:24425, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6387] Another function of VGAM23 is therefore inhibition of FLJ14327 (Accession NM_024912). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14327. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM23 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FYCO1 BINDING SITE, designated SEQ ID:23708, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6388] Another function of VGAM23 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. KIAA0125 (Accession XM_018203) is another VGAM23 host target gene. KIAA0125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0125 BINDING SITE, designated SEQ ID:30346, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6389] Another function of VGAM23 is therefore inhibition of KIAA0125 (Accession XM_018203). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0125. KIAA0202 (Accession XM_034872) is another VGAM23 host target gene. KIAA0202 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0202, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0202 BINDING SITE, designated SEQ ID:32180, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6390] Another function of VGAM23 is therefore inhibition of KIAA0202 (Accession XM_034872). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0202. KIAA0748 (Accession NM_014796) is another VGAM23 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16703, to the nucleotide sequence of VGAM23 RNA, herein designated

VGAM RNA, also designated SEQ ID:2734.

[6391] Another function of VGAM23 is therefore inhibition of KIAA0748 (Accession NM_014796). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. N4BP3 (Accession XM_038920) is another VGAM23 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32939, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6392] Another function of VGAM23 is therefore inhibition of N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. PRO1770 (Accession NM_014100) is another VGAM23 host target gene. PRO1770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1770, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1770 BINDING SITE, designated SEQ ID:15325, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6393] Another function of VGAM23 is therefore inhibition of PRO1770 (Accession NM_014100). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1770. Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM_003342) is another VGAM23 host target gene. UBE2G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G1 BINDING SITE, designated SEQ ID:9347, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6394] Another function of VGAM23 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C.*

elegans) (UBE2G1, Accession NM_003342). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G1. Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM_080872) is another VGAM23 host target gene. UNC5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC5D BINDING SITE, designated SEQ ID:28117, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6395] Another function of VGAM23 is therefore inhibition of Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM_080872). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5D. Voltage-dependent Anion Channel 3 (VDAC3, Accession NM_005662) is another VGAM23 host target gene. VDAC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VDAC3, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDAC3 BINDING SITE, designated SEQ ID:12204, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6396] Another function of VGAM23 is therefore inhibition of Voltage-dependent Anion Channel 3 (VDAC3, Accession NM_005662). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDAC3. LOC145980 (Accession XM_096914) is another VGAM23 host target gene.

LOC145980 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145980 BINDING SITE, designated SEQ ID:40651, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6397] Another function of VGAM23 is therefore inhibition of LOC145980 (Accession XM_096914). Accordingly, utilities

of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145980. LOC150372 (Accession XM_086893) is another VGAM23 host target gene. LOC150372 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150372 BINDING SITE, designated SEQ ID:38939, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6398] Another function of VGAM23 is therefore inhibition of LOC150372 (Accession XM_086893). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150372. LOC157860 (Accession XM_098832) is another VGAM23 host target gene. LOC157860 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC157860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC157860 BINDING SITE, designated SEQ ID:41862, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6399] Another function of VGAM23 is therefore inhibition of LOC157860 (Accession XM_098832). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157860. LOC167147 (Accession XM_094310) is another VGAM23 host target gene. LOC167147 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC167147, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC167147 BINDING SITE, designated SEQ ID:40228, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6400] Another function of VGAM23 is therefore inhibition of LOC167147 (Accession XM_094310). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC167147. LOC201626 (Accession XM_114349) is another VGAM23 host target gene. LOC201626 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201626, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201626 BINDING SITE, designated SEQ ID:42891, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6401] Another function of VGAM23 is therefore inhibition of LOC201626 (Accession XM_114349). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201626. LOC90249 (Accession XM_030300) is another VGAM23 host target gene. LOC90249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90249 BINDING SITE, designated SEQ ID:31010, to the nucleotide sequence of VGAM23 RNA, herein designated VGAM RNA, also designated SEQ ID:2734.

[6402] Another function of VGAM23 is therefore inhibition of

LOC90249 (Accession XM_030300). Accordingly, utilities of VGAM23 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 24 (VGAM24) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6403] VGAM24 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM24 was detected is described hereinabove with reference to Figs. 1–8.

[6404] VGAM24 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6405] VGAM24 gene encodes a VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM24 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM24 precursor RNA is designated SEQ ID:10, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:10 is located at position 107686 relative to the genome of Invertebrate Iridescent Virus 6.

[6406] VGAM24 precursor RNA folds onto itself, forming VGAM24 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6407] An enzyme complex designated DICER COMPLEX, `dices` the VGAM24 folded precursor RNA into VGAM24 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide se-

quence of VGAM24 RNA is designated SEQ ID:2735, and is provided hereinbelow with reference to the sequence listing part.

[6408] VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM24 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[6409] VGAM24 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM24 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustrat-

tion only, and is not meant to be limiting – VGAM24 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6410] The complementary binding of VGAM24 RNA, herein designated VGAM RNA, to host target binding sites on VGAM24 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM24 host target RNA into VGAM24 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6411] It is appreciated that VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM24 host target genes. The mRNA of each one of this plurality of VGAM24 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM24 RNA, herein designated VGAM RNA, and which when bound by VGAM24 RNA causes inhibition of translation of respective one or more VGAM24 host target proteins.

- [6412] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM24 gene, herein designated VGAM GENE, on one or more VGAM24 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [6413] It is yet further appreciated that a function of VGAM24 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM24 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM24 correlate with, and may be deduced from, the identity of the host target genes which VGAM24 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6414] Nucleotide sequences of the VGAM24 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM24 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM24 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM24 are further described hereinbelow with reference to Table 1.

[6415] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM24 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM24 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6416] As mentioned hereinabove with reference to Fig. 1, a function of VGAM24 gene, herein designated VGAM is in-

hibition of expression of VGAM24 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM24 correlate with, and may be deduced from, the identity of the target genes which VGAM24 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6417] Dihydropyrimidinase-like 3 (DPYSL3, Accession NM_001387) is a VGAM24 host target gene. DPYSL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYSL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL3 BINDING SITE, designated SEQ ID:7070, to the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, also designated SEQ ID:2735.

[6418] A function of VGAM24 is therefore inhibition of Dihydropyrimidinase-like 3 (DPYSL3, Accession NM_001387), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL3. The function of DPYSL3 has been established by previous studies. Hamajima et al.

(1996) isolated a cDNA encoding dihydropyrimidinase-like 3 (OMIM Ref. No. DPYSL3), called DRP3 by them, from a fetal brain cDNA library (see OMIM Ref. No. 222748). By Northern blot analysis of adult human tissues, they detected a 5.8-kb DPYSL3 transcript at high levels in heart and skeletal muscle and at low levels in brain and lung. Gaetano et al. (1997) isolated a human ULIP cDNA from retinoic acid-differentiated neuroblastoma cells. In contrast to Hamajima et al. (1996), they found that the gene is expressed strongly in human fetal brain and spinal cord but is not detectably expressed in adult brain and non-neuronal tissues. The 5.5-kb full-length cDNA contains a 1,710-bp open reading frame predicting a 570-amino acid protein. The human gene shares 98% identity with mouse Ulip. The authors speculated that the human ULIP gene mediates signals involved in axonal growth.

[6419] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6420] Hamajima, N.; Matsuda, K.; Sakata, S.; Tamaki, N.; Sasaki, M.; Nonaka, M. : A novel gene family defined by human dihydropyrimidinase and three related proteins with differential tissue distribution. *Gene* 180: 157-163, 1996. ;

and

- [6421] Gaetano, C; Matsuo, T.; Thiele, C. J. : Identification and characterization of a retinoic acid-regulated human homologue of the unc-33-like phosphoprotein gene (hUlip) from neuroblastom.
- [6422] Further studies establishing the function and utilities of DPYSL3 are found in John Hopkins OMIM database record ID 601168, and in cited publications numbered 9303, 930 and 9308 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibroblast Growth Factor 23 (FGF23, Accession NM_020638) is another VGAM24 host target gene. FGF23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF23 BINDING SITE, designated SEQ ID:21796, to the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, also designated SEQ ID:2735.
- [6423] Another function of VGAM24 is therefore inhibition of Fibroblast Growth Factor 23 (FGF23, Accession NM_020638), a gene which a member of the fibroblast

growth factor family . Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF23. The function of FGF23 has been established by previous studies. The FGF23 gene encodes a member of the fibroblast growth factor family that is mutant in autosomal dominant hypophosphatemic rickets (OMIM Ref. No. 193100). Using the mouse Fgf23 sequence as query, Yamashita et al. (2000) identified FGF23 in a genomic database. They cloned the full-length cDNA from a placenta library. The deduced 251-amino acid protein contains an N-terminal 24-amino acid signal sequence. FGF23 shares 72% sequence identity with mouse Fgf23, and 24% and 22% identity with human FGF21 and FGF19, respectively. By quantitative PCR, Yamashita et al. (2000) found highest expression of Fgf23 in mouse brain and lower expression in thymus. In situ hybridization of mouse brain revealed discrete specific labeling only in the ventrolateral thalamic nucleus. Autosomal dominant hypophosphatemic rickets (ADHR; 193100) is characterized by low serum phosphorus concentrations, rickets, osteomalacia, leg deformities, short stature, bone pain, and dental abscesses. The ADHR Consortium (2000) described a positional cloning ap-

proach used to identify the gene mutated in ADHR. They identified mutations in the FGF23 gene in affected members of families segregating ADHR. The ADHR Consortium (2000) found that the FGF23 gene lies 54 kb telomeric of FGF6 (OMIM Ref. No. 134921) on 12p13.

- [6424] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [6425] Yamashita, T.; Yoshioka, M.; Itoh, N. : Identification of a novel fibroblast growth factor, FGF-23, preferentially expressed in the ventrolateral thalamic nucleus of the brain. *Biochem. Biophys. Res. Commun.* 277: 494-498, 2000. ; and
- [6426] ADHR Consortium : Autosomal dominant hypophosphataemic rickets is associated with mutations in FGF23. *Nature Genet.* 26: 345-348, 2000.
- [6427] Further studies establishing the function and utilities of FGF23 are found in John Hopkins OMIM database record ID 605380, and in cited publications numbered 1 and 6989-6993 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glycine Amidinotransferase (L-arginine:glycine amidinotransferase) (GATM, Accession NM_001482) is another VGAM24

host target gene. GATM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATM BINDING SITE, designated SEQ ID:7224, to the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, also designated SEQ ID:2735.

[6428] Another function of VGAM24 is therefore inhibition of Glycine Amidinotransferase (L-arginine:glycine amidinotransferase) (GATM, Accession NM_001482), a gene which glycine amidinotransferase; component of the creatine biosynthetic pathway. Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATM. The function of GATM has been established by previous studies. Creatine and phosphocreatine play important roles in the energy metabolism of muscle and nerve tissues. The enzyme L-arginine:glycine amidinotransferase (AGAT; EC 2.1.4.1) catalyzes the transfer of a guanido group from arginine to glycine, forming guanidinoacetic acid, the immediate precursor of creatine. One of the major sites of creatine

biosynthesis is the kidney. Humm et al. (1994) isolated and sequenced AGAT from pig kidney mitochondria. Sequence data from the pig AGAT polypeptide allowed them to isolate cDNA clones encoding the human enzyme from a kidney carcinoma cDNA library. The largest human cDNA sequence encodes a 423-amino acid polypeptide including a 37-amino acid signal sequence. The mature porcine and human proteins are 94% identical to each other and 36% identical to bacterial L-arginine:inosamine phosphate amidinotransferase. Humm et al. (1997) noted that mitochondrial and cytosolic forms of AGAT are believed to derive from the same gene by alternative splicing. They expressed human AGAT in *E. coli* and identified its active-site cysteine residue (OMIM Ref. No. cys407). Item et al. (2001) described AGAT deficiency in 2 sisters, aged 4 and 6 years, with mental retardation and severe creatine deficiency in the brain, reported by Bianchi et al. (2000). The brain creatine deficiency in the sibs was reversible by means of oral creatine supplementation. Urinary guanidinoacetate concentrations were low. Item et al. (2001) found a homozygous G-to-A transition at nucleotide position 9297, converting a tryptophan codon (TGG) to a stop codon (TAG) at residue 149 (T149X;

602360.0001), and resulting in undetectable cDNA, as investigated by RT-PCR, as well as in undetectable AGAT activity, as investigated radiochemically in cultivated skin fibroblasts and in virus-transformed lymphoblasts of the patients. The parents were heterozygous for the mutant allele, with intermediate residual AGAT activities.

[6429] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6430] Humm, A.; Fritsche, E.; Mann, K.; Gohl, M.; Huber, R. : Recombinant expression and isolation of human L-arginine:glycine amidinotransferase and identification of its active-site cysteine residue. *Biochem. J.* 322: 771-776, 1997. ; and

[6431] Item, C. B.; Stockler-Ipsiroglu, S.; Stromberger, C.; Muhl, A.; Alessandri, M. G.; Bianchi, M. C.; Tosetti, M.; Fornai, F.; Cioni, G. : Arginine:glycine amidinotransferase deficiency: th.

[6432] Further studies establishing the function and utilities of GATM are found in John Hopkins OMIM database record ID 602360, and in cited publications numbered 8534-8537 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. IPT (Accession

NM_017646) is another VGAM24 host target gene. IPT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IPT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IPT BINDING SITE, designated SEQ ID:19152, to the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, also designated SEQ ID:2735.

[6433] Another function of VGAM24 is therefore inhibition of IPT (Accession NM_017646). Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IPT. ShrmL (Accession NM_020859) is another VGAM24 host target gene. ShrmL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ShrmL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ShrmL BINDING SITE, designated SEQ ID:21912, to the nucleotide sequence of VGAM24 RNA, herein designated VGAM RNA, also designated SEQ ID:2735.

- [6434] Another function of VGAM24 is therefore inhibition of ShrmL (Accession NM_020859). Accordingly, utilities of VGAM24 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ShrmL. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 25 (VGAM25) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [6435] VGAM25 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM25 was detected is described hereinabove with reference to Figs. 1–8.
- [6436] VGAM25 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [6437] VGAM25 gene encodes a VGAM25 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM25 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM25 precursor RNA is designated SEQ ID:11, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:11 is located at position 11733 relative to the genome of Invertebrate Iridescent Virus 6.

[6438] VGAM25 precursor RNA folds onto itself, forming VGAM25 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6439] An enzyme complex designated DICER COMPLEX, `dices` the VGAM25 folded precursor RNA into VGAM25 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM25 RNA is designated SEQ ID:2736, and is provided hereinbelow with reference to the sequence listing part.

[6440] VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM25 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[6441] VGAM25 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM25 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustra-

tion only, and is not meant to be limiting – VGAM25 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6442] The complementary binding of VGAM25 RNA, herein designated VGAM RNA, to host target binding sites on VGAM25 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM25 host target RNA into VGAM25 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6443] It is appreciated that VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM25 host target genes. The mRNA of each one of this plurality of VGAM25 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM25 RNA, herein designated VGAM RNA, and which when bound by VGAM25 RNA causes inhibition of translation of respective one or more VGAM25 host target proteins.

- [6444] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM25 gene, herein designated VGAM GENE, on one or more VGAM25 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [6445] It is yet further appreciated that a function of VGAM25 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM25 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM25 correlate with, and may be deduced from, the identity of the host target genes which VGAM25 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6446] Nucleotide sequences of the VGAM25 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM25 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM25 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM25 are further described hereinbelow with reference to Table 1.

[6447] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM25 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM25 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6448] As mentioned hereinabove with reference to Fig. 1, a function of VGAM25 gene, herein designated VGAM is in-

hibition of expression of VGAM25 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM25 correlate with, and may be deduced from, the identity of the target genes which VGAM25 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6449] Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502) is a VGAM25 host target gene. CX3CR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CX3CR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CX3CR1 BINDING SITE, designated SEQ ID:34979, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6450] A function of VGAM25 is therefore inhibition of Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502), a gene which mediates both the adhesive and migratory functions of fractalkine. Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CX3CR1. The function of CX3CR1 has been established by previous studies. Leukocyte trafficking at the endothelium requires both cellular adhesion molecules and chemotactic factors. Fractalkine (OMIM Ref. No. 601880), a transmembrane molecule with a CX3C-motif chemokine domain atop a mucin stalk, induces both adhesion and migration of leukocytes. Imai et al. (1997) identified a 7-transmembrane high-affinity receptor for fractalkine and showed that it mediates both the adhesive and migratory functions of fractalkine. The receptor, which the authors termed CX3CR1, requires pertussis toxin-sensitive G protein signaling to induce migration but not to support adhesion, which also occurs without other adhesion molecules but requires the architecture of a chemokine domain atop the mucin stalk. Natural killer cells predominantly express CX3CR1 and respond to fractalkine in both migration and adhesion. Imai et al. (1997) concluded that fractalkine and CX3CR1 represent new types of leukocyte trafficking regulators, performing both adhesive and chemotactic functions. CX3CR1 is an HIV coreceptor as well as a leukocyte chemotactic/adhesion receptor for fractalkine. Faure et al. (2000) identified 2 single nucleotide polymorphisms in the CX3CR1 gene in

Caucasians and demonstrated that HIV-infected patients homozygous for I249/M280 (601470.0001) progressed to AIDS more rapidly than those with other haplotypes (relative risk = 2.13, $P = 0.039$). Functional CX3CR1 analysis showed that fractalkine binding is reduced among patients homozygous for this particular haplotype. Thus, Faure et al. (2000) concluded that CX3CR1-I249/M280 is a recessive genetic risk factor for HIV/AIDS. Tripp et al. (2001) showed that the G glycoprotein of respiratory syncytial virus (RSV) shares a heparin-binding domain and a CX3C chemokine motif with CX3CL1. Binding analysis indicated that RSV can use CX3CR1 as a receptor. G glycoprotein binding mimics fractalkine binding and induces leukocyte chemotaxis. Tripp et al. (2001) concluded that RSV G glycoprotein uses its similarities with CX3C to facilitate infection and to modify the immune response.

[6451] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6452] Faure, S.; Meyer, L.; Costagliola, D.; Vaneensberghe, C.; Genin, E.; Autran, B.; French ALT and IMMUNOCO Study Groups; Delfraissy, J.-F.; SEROCO Study Group; McDermott, D. H.; Murphy, P. M.; Debre, P.; Theodorou, I.; Cam-

badiere, C. : Rapid progression to AIDS in HIV+ individuals with a structural variant of the chemokine receptor CX(3)CR1. Science 287: 2274–2277, 2000. ; and

[6453] Moatti, D.; Faure, S.; Fumeron, F.; Amara, M. E. W.; Sek-nadji, P.; McDermott, D. H.; Debre, P.; Aumont, M. C.; Murphy, P. M.; de Prost, D.; Combadiere, C. : Polymorphism in the fractalk.

[6454] Further studies establishing the function and utilities of CX3CR1 are found in John Hopkins OMIM database record ID 601470, and in cited publications numbered 6694–669 and 8093–6698 listed in the bibliography section herein–below, which are also hereby incorporated by reference.F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_033644) is another VGAM25 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:27370, SEQ ID:27380 and SEQ ID:14668 respectively, to the nucleotide sequence of VGAM25 RNA,

herein designated VGAM RNA, also designated SEQ ID:2736.

[6455] Another function of VGAM25 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_033644), a gene which somehow is involved in the process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B has been established by previous studies. Using a yeast 2-hybrid screen with SKP1 as bait, followed by searching sequence databases, Winston et al. (1999) and Cenciarelli et al. (1999) identified 33 mammalian and 26 human F-box proteins, respectively. These contained C termini with leucine-rich repeats (FBXLs, e.g., SKP2 (OMIM Ref. No. 601436)), WD40 domains (FBXWs, e.g., BTRCP (OMIM Ref. No. 603482)), or no recognizable motifs (FBXOs, e.g., CCNF). By searching an EST database for homologs of BTRCP, followed by RT-PCR on gastric cancer cell lines and screening fetal brain and fetal lung cDNA libraries, Koike et al. (2000) obtained cDNAs encoding 3 isoforms of FBXW1B, which they termed BTRCP2A, BTRCP2B, and BTRCP2C. Sequence analysis predicted that the 3 isoforms

share the same N-terminal 15 amino acids, F box, and 7 C-terminal WD repeats. The 525-amino acid BTRCP2B protein has a 21-amino acid insert after met15 of the 508-amino acid BTRCP2A protein, and BTRCP2C has a 34-amino acid insert after met15 of BTRCP2A. BTRCP2A is 86% identical to BTRCP. BTRCP2C is nearly identical to the KIAA0696 protein identified by Ishikawa et al. (1998). By genomic sequence analysis, Koike et al. (2000) determined that the FBXW1B gene contains at least 14 exons, with BTRCP2A lacking exons 2 and 3, BTRCP2B lacking exon 2, and BTRCP2C lacking exon 3. Northern blot analysis revealed near ubiquitous expression of a 4.5-kb transcript. By RT-PCR analysis, Ishikawa et al. (1998) detected expression in all tissues tested except spleen.

[6456] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6457] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 5: 169–176, 1998. ; and

[6458] Koike, J.; Sagara, N.; Kirikoshi, H.; Takagi, A.; Miwa, T.; Hirai, M.; Katoh, M. : Molecular cloning and genomic structure of the beta-TRCP2 gene on chromosome 5q35.1. Biochem. Biophys.

[6459] Further studies establishing the function and utilities of FBXW1B are found in John Hopkins OMIM database record ID 605651, and in cited publications numbered 40 and 9440 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621) is another VGAM25 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10978, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6460] Another function of VGAM25 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621), a gene which

has calcium channel activity. Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 has been established by previous studies. TRPCs, mammalian homologs of the *Drosophila* transient receptor potential (*trp*) protein, are ion channels that are thought to mediate capacitative calcium entry into the cell. Using a PCR-based strategy, Hofmann et al. (1999) isolated cDNAs encoding TRPC6, a novel member of the TRPC family. The predicted 931-amino acid protein shares 93% identity with mouse *Trpc6*. The authors found that TRPC6 is a nonselective cation channel that is activated by diacylglycerol (DAG) in a membrane-delimited fashion, independently of protein kinase C. Although TRPC3 (OMIM Ref. No. 602345), the closest structural relative of TRPC6, is activated in the same manner, human TRPC1 and mouse *Trpc4* (OMIM Ref. No. 603651) and *Trpc5* (OMIM Ref. No. 300334) were unresponsive to DAG. The authors suggested that TRPC3 and TRPC6 represent the first members of a new functional family of second-messenger-operated cation channels that are activated by DAG. Northern blot analysis revealed that TRPC6 is expressed primarily in placenta, lung, spleen, ovary, and

small intestine. By FISH, D'Esposito et al. (1998) mapped the TRPC6 gene to chromosome 11q21–q22.

[6461] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6462] Hofmann, T.; Obukhov, A. G.; Schaefer, M.; Harteneck, C.; Gudermann, T.; Schultz, G. : Direct activation of human TRPC6 and TRPC3 channels by diacylglycerol. *Nature* 397: 259–263, 1999. ; and

[6463] D'Esposito, M.; Strazzullo, M.; Cuccurese, M.; Spalluto, C.; Rocchi, M.; D'Urso, M.; Ciccodicola, A. : Identification and assignment of the human transient receptor potential channel 6 gene.

[6464] Further studies establishing the function and utilities of TRPC6 are found in John Hopkins OMIM database record ID 603652, and in cited publications numbered 5857–5858 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 135 (clone pHZ–17) (ZNF135, Accession NM_003436) is another VGAM25 host target gene. ZNF135 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF135, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF135 BINDING SITE, designated SEQ ID:9490, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6465] Another function of VGAM25 is therefore inhibition of Zinc Finger Protein 135 (clone pHZ-17) (ZNF135, Accession NM_003436). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF135. BCL2-associated Athanogene 2 (BAG2, Accession XM_165779) is another VGAM25 host target gene. BAG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG2 BINDING SITE, designated SEQ ID:43753, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6466] Another function of VGAM25 is therefore inhibition of BCL2-associated Athanogene 2 (BAG2, Accession

XM_165779). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG2. FLJ12649 (Accession NM_024597) is another VGAM25 host target gene.

FLJ12649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12649 BINDING SITE, designated SEQ ID:23835, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6467] Another function of VGAM25 is therefore inhibition of FLJ12649 (Accession NM_024597). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12649. GFR (Accession NM_012294) is another VGAM25 host target gene. GFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of GFR BINDING SITE, designated SEQ ID:14642, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6468] Another function of VGAM25 is therefore inhibition of GFR (Accession NM_012294). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. KIAA0626 (Accession NM_021647) is another VGAM25 host target gene. KIAA0626 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0626, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0626 BINDING SITE, designated SEQ ID:22313, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6469] Another function of VGAM25 is therefore inhibition of KIAA0626 (Accession NM_021647). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0626. PRO0902 (Accession NM_053057) is another VGAM25 host target gene. PRO0902 BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO0902, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0902 BINDING SITE, designated SEQ ID:27608, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6470] Another function of VGAM25 is therefore inhibition of PRO0902 (Accession NM_053057). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0902. Syntaxin 12 (STX12, Accession XM_039018) is another VGAM25 host target gene. STX12 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by STX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STX12 BINDING SITE, designated SEQ ID:32983, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6471] Another function of VGAM25 is therefore inhibition of

Syntaxin 12 (STX12, Accession XM_039018). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STX12. SZF1 (Accession NM_016089) is another VGAM25 host target gene. SZF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SZF1 BINDING SITE, designated SEQ ID:18173, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6472] Another function of VGAM25 is therefore inhibition of SZF1 (Accession NM_016089). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SZF1. LOC143879 (Accession XM_084666) is another VGAM25 host target gene. LOC143879 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC143879 BINDING SITE, designated SEQ ID:37662, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6473] Another function of VGAM25 is therefore inhibition of LOC143879 (Accession XM_084666). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143879. LOC158954 (Accession XM_017340) is another VGAM25 host target gene. LOC158954 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158954 BINDING SITE, designated SEQ ID:30313, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6474] Another function of VGAM25 is therefore inhibition of LOC158954 (Accession XM_017340). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158954. LOC200609 (Accession XM_117256) is an-

other VGAM25 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43333, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6475] Another function of VGAM25 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC50999 (Accession NM_016040) is another VGAM25 host target gene. LOC50999 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC50999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC50999 BINDING SITE, designated SEQ ID:18118, to the nucleotide sequence of VGAM25 RNA, herein designated VGAM RNA, also designated SEQ ID:2736.

[6476] Another function of VGAM25 is therefore inhibition of LOC50999 (Accession NM_016040). Accordingly, utilities of VGAM25 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC50999. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 26 (VGAM26) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6477] VGAM26 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM26 was detected is described hereinabove with reference to Figs. 1–8.

[6478] VGAM26 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6479] VGAM26 gene encodes a VGAM26 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM26

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM26 precursor RNA is designated SEQ ID:12, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:12 is located at position 77256 relative to the genome of Invertebrate Iridescent Virus 6.

[6480] VGAM26 precursor RNA folds onto itself, forming VGAM26 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6481] An enzyme complex designated DICER COMPLEX, `dices` the VGAM26 folded precursor RNA into VGAM26 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 40%) nucleotide sequence of VGAM26 RNA is designated SEQ ID:2737, and is provided hereinbelow with reference to the sequence listing part.

[6482] VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM26 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6483] VGAM26 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM26 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host tar-

get binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM26 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6484] The complementary binding of VGAM26 RNA, herein designated VGAM RNA, to host target binding sites on VGAM26 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM26 host target RNA into VGAM26 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6485] It is appreciated that VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM26 host target genes. The mRNA of each one of this plurality of VGAM26 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM26 RNA, herein designated VGAM RNA, and which when bound by VGAM26 RNA causes inhibition of translation of respective one or more VGAM26 host target proteins.

[6486] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM26 gene, herein designated VGAM GENE, on one or more VGAM26 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6487] It is yet further appreciated that a function of VGAM26 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM26 correlate with, and may be deduced from, the identity of the host target genes which VGAM26 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6488] Nucleotide sequences of the VGAM26 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM26 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM26 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM26 are further described hereinbelow with reference to Table 1.

[6489] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM26 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM26 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6490] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM26 gene, herein designated VGAM is inhibition of expression of VGAM26 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM26 correlate with, and may be deduced from, the identity of the target genes which VGAM26 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6491] CRACC (Accession NM_021181) is a VGAM26 host target gene. CRACC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRACC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRACC BINDING SITE, designated SEQ ID:22154, to the nucleotide sequence of VGAM26 RNA, herein designated VGAM RNA, also designated SEQ ID:2737.

[6492] A function of VGAM26 is therefore inhibition of CRACC (Accession NM_021181), a gene which may participate in adhesion reactions between T lymphocytes and accessory cells. Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRACC. The function of CRACC has

been established by previous studies. Natural killer (NK)-cell function is regulated by a balance between signaling through inhibitory (e.g., KIR2DL1; 604936) and activating receptors. Some members of the CD2 (OMIM Ref. No. 186990) family of activating receptors (e.g., CD244; 605554) stimulate cytotoxicity through the SLAM (OMIM Ref. No. 603492)-associated protein (SAP; 308240). Mutations in the SH2 domain of SAP cause deficiencies in other CD2 family proteins that transduce signals through SAP, and these deficiencies lead to uncontrolled Epstein-Barr virus (EBV) infections and, ultimately, to X-linked lymphoproliferative disease (XLPD; 308240 Bouchon et al. (2001) also cloned CS1, which they termed CRACC. They noted the presence of 2 CD2-like Ig folds in the extracellular domain of CRACC. RT-PCR analysis detected CRACC expression in NK and CD8 (see OMIM Ref. No. 186910)-positive cytotoxic cells. Flow cytometric analysis demonstrated expression of CRACC on nearly all NK cells, a large subset of CD8 cells, and few CD4 (OMIM Ref. No. 186940) cells and B cells. Expression on B cells was up-regulated upon CD40 (OMIM Ref. No. 109535) activation, and expression on dendritic cells was upregulated by influenza virus, lipopolysaccharide, and CD40L (OMIM Ref.

No. 300386). Immunoprecipitation and SDS-PAGE analyses showed expression of a 66-kD protein and, after deglycosylation, a 37-kD protein. Functional analysis indicated that CRACC mediates lysis that is in addition to that mediated by NKP46 (OMIM Ref. No. 604530) or CD16 (OMIM Ref. No. 146740). Further analysis determined that, unlike CD244, cytotoxicity mediated by CRACC or NKP46 is SAP-independent and that CRACC triggers ERK (see OMIM Ref. No. 601335) activation. Immunoblot analysis showed that CRACC is tyrosine phosphorylated in activated NK cells and is associated with 19- and 39-kD proteins. Bouchon et al. (2001) proposed that CRACC may be particularly important in controlling pathogens other than EBV

[6493] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6494] Bouchon, A.; Cella, M.; Grierson, H. L.; Cohen, J. I.; Colonna, M. : Cutting edge: activation of NK cell-mediated cytotoxicity by a SAP-independent receptor of the CD2 family. *J. Immun.* 167: 5517-5521, 2001. ; and

[6495] Boles, K. S.; Mathew, P. A. : Molecular cloning of CS1, a novel human natural killer cell receptor belonging to the

CD2 subset of the immunoglobulin superfamily. Immunogenetics 52: 302–.

[6496] Further studies establishing the function and utilities of CRACC are found in John Hopkins OMIM database record ID 606625, and in cited publications numbered 4520–4521 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14351 (Accession NM_024732) is another VGAM26 host target gene. FLJ14351 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14351 BINDING SITE, designated SEQ ID:24073, to the nucleotide sequence of VGAM26 RNA, herein designated VGAM RNA, also designated SEQ ID:2737.

[6497] Another function of VGAM26 is therefore inhibition of FLJ14351 (Accession NM_024732). Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14351. KIAA0102 (Accession NM_014752) is another VGAM26 host target gene. KIAA0102 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA0102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0102 BINDING SITE, designated SEQ ID:16477, to the nucleotide sequence of VGAM26 RNA, herein designated VGAM RNA, also designated SEQ ID:2737.

[6498] Another function of VGAM26 is therefore inhibition of KIAA0102 (Accession NM_014752). Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0102. Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM_047536) is another VGAM26 host target gene. OBSCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OBSCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OBSCN BINDING SITE, designated SEQ ID:34987, to the nucleotide sequence of VGAM26 RNA, herein designated VGAM RNA, also designated SEQ ID:2737.

[6499] Another function of VGAM26 is therefore inhibition of Obscurin, Cytoskeletal Calmodulin and Titin-interacting RhoGEF (OBSCN, Accession XM_047536). Accordingly, utilities of VGAM26 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OBSCN. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 27 (VGAM27) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6500] VGAM27 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM27 was detected is described hereinabove with reference to Figs. 1–8.

[6501] VGAM27 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6502] VGAM27 gene encodes a VGAM27 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM27 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM27 precursor RNA is designated SEQ ID:13, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:13 is located at position 12904 relative to the genome of Invertebrate Iridescent Virus 6.

[6503] VGAM27 precursor RNA folds onto itself, forming VGAM27 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6504] An enzyme complex designated DICER COMPLEX, `dices` the VGAM27 folded precursor RNA into VGAM27 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM27 RNA is designated SEQ ID:2738, and is provided hereinbelow with reference to the sequence listing part.

[6505] VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM27 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[6506] VGAM27 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM27 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM27 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6507] The complementary binding of VGAM27 RNA, herein designated VGAM RNA, to host target binding sites on VGAM27 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM27 host target RNA into VGAM27 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6508] It is appreciated that VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM27 host target genes. The mRNA of each one of this plurality of VGAM27 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM27 RNA, herein designated VGAM RNA, and which when bound by VGAM27 RNA causes inhibition of translation of respective one or more VGAM27 host target proteins.

[6509] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM27 gene, herein designated VGAM GENE, on one or more VGAM27 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6510] It is yet further appreciated that a function of VGAM27 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM27 correlate with, and may be deduced from, the identity of the host target genes which VGAM27 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6511] Nucleotide sequences of the VGAM27 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM27 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM27 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM27 are further described hereinbelow with reference to Table 1.

[6512] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM27 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM27 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6513] As mentioned hereinabove with reference to Fig. 1, a function of VGAM27 gene, herein designated VGAM is inhibition of expression of VGAM27 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM27 correlate with, and may be deduced from, the identity of the target genes which VGAM27 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6514] FLJ14600 (Accession NM_032810) is a VGAM27 host target gene. FLJ14600 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14600 BINDING SITE, designated SEQ ID:26573, to the nucleotide sequence of VGAM27 RNA, herein designated VGAM RNA, also designated SEQ ID:2738.

[6515] A function of VGAM27 is therefore inhibition of FLJ14600 (Accession NM_032810). Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14600.

KIAA0215 (Accession NM_014735) is another VGAM27

host target gene. KIAA0215 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0215, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0215 BINDING SITE, designated SEQ ID:16385, to the nucleotide sequence of VGAM27 RNA, herein designated VGAM RNA, also designated SEQ ID:2738.

[6516] Another function of VGAM27 is therefore inhibition of KIAA0215 (Accession NM_014735). Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0215. NFASC (Accession XM_046808) is another VGAM27 host target gene. NFASC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFASC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFASC BINDING SITE, designated SEQ ID:34833, to the nucleotide sequence of VGAM27 RNA, herein designated VGAM RNA, also designated SEQ ID:2738.

[6517] Another function of VGAM27 is therefore inhibition of NFASC (Accession XM_046808). Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFASC. Phosphodiesterase 10A (PDE10A, Accession NM_006661) is another VGAM27 host target gene. PDE10A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE10A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE10A BINDING SITE, designated SEQ ID:13464, to the nucleotide sequence of VGAM27 RNA, herein designated VGAM RNA, also designated SEQ ID:2738.

[6518] Another function of VGAM27 is therefore inhibition of Phosphodiesterase 10A (PDE10A, Accession NM_006661). Accordingly, utilities of VGAM27 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE10A. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 28 (VGAM28) viral gene, which modulates expression of respective host target

genes thereof, the function and utility of which host target genes is known in the art.

[6519] VGAM28 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM28 was detected is described hereinabove with reference to Figs. 1–8.

[6520] VGAM28 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6521] VGAM28 gene encodes a VGAM28 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM28 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM28 precursor RNA is designated SEQ ID:14, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:14 is located at position 90871 relative to the genome of Invertebrate Iridescent Virus 6.

[6522] VGAM28 precursor RNA folds onto itself, forming VGAM28 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6523] An enzyme complex designated DICER COMPLEX, `dices` the VGAM28 folded precursor RNA into VGAM28 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM28 RNA is designated SEQ ID:2739, and is provided hereinbelow with reference to the sequence listing part.

[6524] VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM28 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6525] VGAM28 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM28 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM28 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[6526] The complementary binding of VGAM28 RNA, herein designated VGAM RNA, to host target binding sites on VGAM28 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM28 host target RNA into VGAM28 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6527] It is appreciated that VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM28 host target genes. The mRNA of each one of this plurality of VGAM28 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM28 RNA, herein designated VGAM RNA, and which when bound by VGAM28 RNA causes inhibition of translation of respective one or more VGAM28 host target proteins.

[6528] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM28 gene, herein designated VGAM GENE, on one or

more VGAM28 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6529] It is yet further appreciated that a function of VGAM28 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM28 correlate with, and may be deduced from, the identity of the host target genes which VGAM28 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6530] Nucleotide sequences of the VGAM28 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM28 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM28 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM28 are further de-
scribed hereinbelow with reference to Table 1.

[6531] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM28 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM28 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[6532] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM28 gene, herein designated VGAM is in-
hibition of expression of VGAM28 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM28 correlate with, and may be deduced from, the
identity of the target genes which VGAM28 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[6533] Cysteine Knot Superfamily 1, BMP Antagonist 1
(CKTSF1B1, Accession NM_013372) is a VGAM28 host tar-

get gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15022, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6534] A function of VGAM28 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 has been established by previous studies. Using a Xenopus expression-cloning screen, Hsu et al. (1998) isolated Gremlin, an antagonist of bone morphogenetic protein (BMP) signaling that is expressed in the neural crest. Gremlin belongs to a novel gene family that includes the head-inducing factor Cerberus (OMIM Ref. No. 603777) and the tumor suppressor DAN (OMIM Ref. No. 600613). Hsu et al. (1998) showed

that all family members are secreted proteins and that they act as BMP antagonists in embryonic explants. They also provided support for the model that Gremlin, Cerberus, and DAN block BMP signaling by binding BMPs, preventing them from interacting with their receptors. They proposed that Gremlin, Cerberus, and DAN control diverse processes in growth and development by selectively antagonizing the activities of different subsets of the transforming growth factor (TGF)-beta ligands. By homology searches, Hsu et al. (1998) cloned the human homolog of *Xenopus* Gremlin. The human gremlin cDNA encodes a predicted 184-amino acid protein. Zuniga et al. (1999) reported that the secreted BMP antagonist Gremlin relays the sonic hedgehog (SHH; 600725) signal from the polarizing region to the apical ectodermal ridge. Mesenchymal Gremlin expression is lost in limb buds of mouse embryos homozygous for the 'limb deformity' (ld) mutation, which disrupts establishment of the Shh/Fgf4 (OMIM Ref. No. 164980) feedback loop. Grafting Gremlin-expressing cells into ld mutant limb buds rescued Fgf4 expression and restored the Shh/Fgf4 feedback loop. Analysis of Shh-null mutant embryos revealed that Shh signaling is required for maintenance of Gremlin and

Formin (OMIM Ref. No. 136535), the gene disrupted by the Id mutations. In contrast, Formin, Gremlin, and Fgf4 activation were independent of Shh signaling. Zuniga et al. (1999) concluded that the study uncovered the cascade by which the SHH signal is relayed from the posterior mesenchyme to the apical ectodermal ridge and established that Formin-dependent activation of the BMP antagonist Gremlin is sufficient to induce Fgf4 and establish the SHH/Fgf4 feedback loop.

[6535] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6536] Hsu, D. R.; Economides, A. N.; Wang, X.; Eimon, P. M.; Harland, R. M. : The *Xenopus* dorsalizing factor gremlin identifies a novel family of secreted proteins that antagonize BMP activities. *Molec. Cell* 1: 673–683, 1998. ; and

[6537] Zuniga, A.; Haramis, A.–P. G.; McMahon, A. P.; Zeller, R. : Signal relay by BMP antagonism controls the SHH/FGF4 feedback loop in vertebrate limb buds. *Nature* 401: 598–602, 1999.

[6538] Further studies establishing the function and utilities of CKTSF1B1 are found in John Hopkins OMIM database record ID 603054, and in cited publications numbered

8017–801 and 2130 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Copine III (CPNE3, Accession NM_003909) is another VGAM28 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9992, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6539] Another function of VGAM28 is therefore inhibition of Copine III (CPNE3, Accession NM_003909), a gene which may function in membrane trafficking. Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 has been established by previous studies. By screening human brain cDNAs for the potential to encode proteins larger than 50 kD, Ishikawa et al. (1998) identified a CPNE3 cDNA, which they called KIAA0636. The deduced 537-amino acid CPNE3 protein is 65.7% identical to CPNE1. By SDS-PAGE, the in vitro tran-

scribed/translated product of the CPNE3 cDNA had a molecular mass of 65 kD. RT-PCR detected CPNE3 expression in all human tissues examined. By immunoprecipitation and kinase assays, Caudell et al. (2000) serendipitously identified a 60-kD protein identical to CPNE3. CPNE3 contains 2 N-terminal C2 domains, like CPNE1, CPNE6 (OMIM Ref. No. 605688), and CPNE7 (OMIM Ref. No. 605689), but these 4 copines have divergent C termini. CPNE3 is 63%, 52%, and 47% identical to CPNE1, CPNE6, and CPNE7, respectively. Northern blot analysis revealed ubiquitous expression of a 5.0-kb transcript. Biochemical analysis showed that CPNE3 appears to possess endogenous kinase activity, although it lacks a classic kinase domain. CPNE3 is phosphorylated on both serine and threonine residues but not on tyrosine residues.

[6540] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6541] Creutz, C. E.; Tomsig, J. L.; Snyder, S. L.; Gautier, M.-C.; Skouri, F.; Beisson, J.; Cohen, J. : The copines, a novel class of C2 domain-containing, calcium-dependent, phospholipid-binding proteins conserved from Paramecium to humans. *J. Biol. Chem.* 273: 1393–1402, 1998. ;

and

- [6542] Caudell, E. G.; Caudell, J. J.; Tang, C.-H.; Yu, T.-K.; Frederick, M. J.; Grimm, E. A. : Characterization of human copine III as a phosphoprotein with associated kinase activity. *Biochem.*
- [6543] Further studies establishing the function and utilities of CPNE3 are found in John Hopkins OMIM database record ID 604207, and in cited publications numbered 475 and 9440 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myosin X (MYO10, Accession NM_012334) is another VGAM28 host target gene. MYO10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO10 BINDING SITE, designated SEQ ID:14730, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.
- [6544] Another function of VGAM28 is therefore inhibition of Myosin X (MYO10, Accession NM_012334), a gene which is an unconventional myosin. Accordingly, utilities of

VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO10. The function of MYO10 has been established by previous studies. See MYO1A (OMIM Ref. No. 601478). By PCR amplification of RNA from porcine and human cell lines and human liver, Bement et al. (1994) identified 8–11 putative myosins representing 6 distinct myosin classes. Among the identified myosins was a cDNA encoding a myosin designated MYO10. Using interspecific backcross mapping, Hasson et al. (1996) mapped the Myo10 gene to mouse chromosome 15 in a region that predicted a location of the human homolog on either 5p14–p12 or 8q22–q23. They showed by fluorescence in situ hybridization that human MYO10 maps to 5p15.1–p14.3.

[6545] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6546] Bement, W. M.; Hasson, T.; Wirth, J. A.; Cheney, R. E.; Mooseker, M. S. : Identification and overlapping expression of multiple unconventional myosin genes in vertebrate cell types. *Proc. Nat. Acad. Sci.* 91: 6549–6553, 1994. Erratum: *Proc. Nat. Acad. Sci.* 91: 11767, 1994. ; and

[6547] Hasson, T.; Skowron, J. F.; Gilbert, D. J.; Avraham, K. B.; Perry, W. L.; Bement, W. M.; Anderson, B. L.; Sherr, E. H.; Chen, Z.-Y.; Greene, L. A.; Ward, D. C.; Corey, D. P.; Mooseker.

[6548] Further studies establishing the function and utilities of MYO10 are found in John Hopkins OMIM database record ID 601481, and in cited publications numbered 651 and 7027 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Kinase C, Nu (PRKCN, Accession NM_005813) is another VGAM28 host target gene. PRKCN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKCN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCN BINDING SITE, designated SEQ ID:12396, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6549] Another function of VGAM28 is therefore inhibition of Protein Kinase C, Nu (PRKCN, Accession NM_005813). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with PRKCN. Eukaryotic Translation Initiation Factor 2C, 2 (EIF2C2, Accession XM_050334) is another VGAM28 host target gene. EIF2C2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EIF2C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C2 BINDING SITE, designated SEQ ID:35613, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6550] Another function of VGAM28 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 2 (EIF2C2, Accession XM_050334). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2C2. FLJ12934 (Accession NM_022899) is another VGAM28 host target gene. FLJ12934 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12934 BINDING SITE, designated

SEQ ID:23174, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6551] Another function of VGAM28 is therefore inhibition of FLJ12934 (Accession NM_022899). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12934. KIAA1701 (Accession XM_042087) is another VGAM28 host target gene. KIAA1701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1701 BINDING SITE, designated SEQ ID:33683, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6552] Another function of VGAM28 is therefore inhibition of KIAA1701 (Accession XM_042087). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1701. Oxysterol Binding Protein-like 10 (OSBPL10, Accession NM_017784) is another VGAM28 host target

gene. OSBPL10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OSBPL10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL10 BINDING SITE, designated SEQ ID:19414, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6553] Another function of VGAM28 is therefore inhibition of Oxysterol Binding Protein-like 10 (OSBPL10, Accession NM_017784). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL10. Synaptophysin-like Protein (SYPL, Accession XM_167511) is another VGAM28 host target gene. SYPL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYPL BINDING SITE, designated SEQ ID:44643, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ

ID:2739.

[6554] Another function of VGAM28 is therefore inhibition of Synaptophysin-like Protein (SYPL, Accession XM_167511). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYPL. LOC120114 (Accession XM_061871) is another VGAM28 host target gene. LOC120114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120114 BINDING SITE, designated SEQ ID:37210, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6555] Another function of VGAM28 is therefore inhibition of LOC120114 (Accession XM_061871). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120114. LOC150848 (Accession XM_097959) is another VGAM28 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41251, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6556] Another function of VGAM28 is therefore inhibition of LOC150848 (Accession XM_097959). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150848. LOC202454 (Accession XM_117400) is another VGAM28 host target gene. LOC202454 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202454 BINDING SITE, designated SEQ ID:43433, to the nucleotide sequence of VGAM28 RNA, herein designated VGAM RNA, also designated SEQ ID:2739.

[6557] Another function of VGAM28 is therefore inhibition of LOC202454 (Accession XM_117400). Accordingly, utilities of VGAM28 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC202454. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 29 (VGAM29) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6558] VGAM29 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM29 was detected is described hereinabove with reference to Figs. 1–8.

[6559] VGAM29 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6560] VGAM29 gene encodes a VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM29 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM29 precursor RNA is designated SEQ

ID:15, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:15 is located at position 3700 relative to the genome of Invertebrate Iridescent Virus 6.

[6561] VGAM29 precursor RNA folds onto itself, forming VGAM29 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6562] An enzyme complex designated DICER COMPLEX, `dices` the VGAM29 folded precursor RNA into VGAM29 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM29 RNA is designated SEQ ID:2740, and is provided hereinbelow with reference to the sequence list-

ing part.

[6563] VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM29 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6564] VGAM29 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM29 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM29 RNA, herein designated VGAM RNA, may have a different num-

ber of host target binding sites in untranslated regions of a VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6565] The complementary binding of VGAM29 RNA, herein designated VGAM RNA, to host target binding sites on VGAM29 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM29 host target RNA into VGAM29 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6566] It is appreciated that VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM29 host target genes. The mRNA of each one of this plurality of VGAM29 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM29 RNA, herein designated VGAM RNA, and which when bound by VGAM29 RNA causes in-

hibition of translation of respective one or more VGAM29 host target proteins.

- [6567] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM29 gene, herein designated VGAM GENE, on one or more VGAM29 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [6568] It is yet further appreciated that a function of VGAM29 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM29 correlate with, and may be deduced from, the identity of the host target genes which VGAM29 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6569] Nucleotide sequences of the VGAM29 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM29 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM29 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM29 are further described hereinbelow with reference to Table 1.

[6570] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM29 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM29 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6571] As mentioned hereinabove with reference to Fig. 1, a function of VGAM29 gene, herein designated VGAM is inhibition of expression of VGAM29 target genes. It is appreciated that specific functions, and accordingly utilities,

of VGAM29 correlate with, and may be deduced from, the identity of the target genes which VGAM29 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6572] Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is a VGAM29 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28938, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6573] A function of VGAM29 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM_002655) is another VGAM29 host target gene. PLAG1 BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by PLAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAG1 BINDING SITE, designated SEQ ID:8515, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6574] Another function of VGAM29 is therefore inhibition of Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM_002655), a gene which contains a zinc finger domain. Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAG1. The function of PLAG1 has been established by previous studies. Pleomorphic adenomas are benign epithelial tumors originating from the major and minor salivary glands (see OMIM Ref. No. 181030). They are characterized by recurrent chromosome translocations; the most common abnormalities involve chromosome 8, with consistent breakpoints at band q12. Kas et al. (1997) described the construction of 2 nonoverlapping YAC contigs covering about 75% of human chromosome band 8q12, which spans approximately 9 Mb of genomic DNA and includes a number of known genes such as MOS

(OMIM Ref. No. 190060) and LYN (OMIM Ref. No. 165120), as well as novel genes and expressed sequence tags (ESTs). By fluorescence in situ hybridization, the authors determined that the majority of pleomorphic adenoma 8q12 breakpoints clustered within a 2-Mb contig that was mapped to the centromeric region of 8q12 and that was covered by 34 overlapping YAC clones, and tagged by 31 markers with an average spacing of 65 kb. Nine of 11 primary adenomas with 8q12 abnormalities had breakpoints mapping within a 300-kb interval. By searching sequence databases with sequence tagged sites (STSs) located within the 300-kb region, Kas et al. (1997) identified an EST with sequence identity to one of the STSs. Northern blot analysis using this EST detected a 7.5-kb transcript representing pleomorphic adenoma gene-1 (PLAG1). The authors cloned human fetal kidney PLAG1 cDNAs and found that the PLAG1 gene contains 5 exons. Southern blot analysis of DNA from pleomorphic adenomas with t(3;8) detected rearrangements in the 5-prime noncoding region of the PLAG1 gene. Using 5-prime RACE or RT-PCR, the authors generated hybrid transcripts consisting of PLAG1 and beta-1-catenin (CTNNB1; 116806) from every primary tumor analyzed. Northern blot analysis of 3

pleomorphic adenomas with t(3;8) and 1 adenoma with a variant t(8;15) revealed that PLAG1 expression was activated by the translocations in all 4 tumors. Kas et al. (1997) detected the 7.5-kb PLAG1 transcript in normal human fetal lung, fetal liver, and fetal kidney, but not in the corresponding adult tissues, adult salivary gland, or fetal brain; CTNNB1 appeared to be ubiquitously expressed. The deduced PLAG1 protein has 2 potential nuclear localization signals in the N-terminal region, 7 zinc finger domains, and a serine-rich C terminus. Astrom et al. (1999) found overexpression of PLAG1 in 23 of 47 primary benign and malignant pleomorphic adenomas of the salivary glands. In 5 adenomas with a normal karyotype, fusion transcripts were found in 3; PLAG1 and CTNNB1 were fused in 1 case, and in 2 others PLAG1 was fused with the gene encoding transcription elongation factor SII (OMIM Ref. No. 601425). The fusions occurred in the 5-prime noncoding region of PLAG1, leading to exchange of regulatory control elements and, as a consequence, activation of PLAG1 gene expression. Because all of the cases had grossly normal karyotypes, the rearrangements must result from cryptic rearrangements.

[6575] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [6576] Astrom, A.-K.; Voz, M. L.; Kas, K.; Roijer, E.; Wedell, B.; Mandahl, N.; Van de Ven, W.; Mark, J.; Stenman, G. : Conserved mechanism of PLAG1 activation in salivary gland tumors with and without chromosome 8q12 abnormalities: identification of SII as a new fusion partner gene. Cancer Res. 59: 918–923, 1999. ; and
- [6577] Kas, K.; Roijer, E.; Voz, M.; Meyen, E.; Stenman, G.; Van de Ven, W. J. M. : A 2–Mb YAC contig and physical map covering the chromosome 8q12 breakpoint cluster region in pleomorphic ad.
- [6578] Further studies establishing the function and utilities of PLAG1 are found in John Hopkins OMIM database record ID 603026, and in cited publications numbered 546 and 5786–5787 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434O125 (Accession XM_036284) is another VGAM29 host target gene. DKFZP434O125 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434O125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates

the complementarity of the nucleotide sequences of DK-FZP434O125 BINDING SITE, designated SEQ ID:32406, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6579] Another function of VGAM29 is therefore inhibition of DK-FZP434O125 (Accession XM_036284). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O125. KIAA0419 (Accession NM_014711) is another VGAM29 host target gene. KIAA0419 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0419, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0419 BINDING SITE, designated SEQ ID:16258, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6580] Another function of VGAM29 is therefore inhibition of KIAA0419 (Accession NM_014711). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0419. KIAA0940 (Accession NM_014912) is another

VGAM29 host target gene. KIAA0940 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0940 BINDING SITE, designated SEQ ID:17146, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6581] Another function of VGAM29 is therefore inhibition of KIAA0940 (Accession NM_014912). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0940. MGC12217 (Accession NM_032771) is another VGAM29 host target gene. MGC12217 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12217, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12217 BINDING SITE, designated SEQ ID:26515, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6582] Another function of VGAM29 is therefore inhibition of MGC12217 (Accession NM_032771). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12217. Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM_015550) is another VGAM29 host target gene. OSBPL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OSBPL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL3 BINDING SITE, designated SEQ ID:17813, to the nucleotide sequence of VGAM29 RNA, herein designated VGAM RNA, also designated SEQ ID:2740.

[6583] Another function of VGAM29 is therefore inhibition of Oxysterol Binding Protein-like 3 (OSBPL3, Accession NM_015550). Accordingly, utilities of VGAM29 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 30 (VGAM30) viral

gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6584] VGAM30 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM30 was detected is described hereinabove with reference to Figs. 1–8.

[6585] VGAM30 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6586] VGAM30 gene encodes a VGAM30 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM30 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM30 precursor RNA is designated SEQ ID:16, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:16 is located at position 128860 relative to the genome of Invertebrate Iridescent Virus 6.

[6587] VGAM30 precursor RNA folds onto itself, forming VGAM30

folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6588] An enzyme complex designated DICER COMPLEX, `dices` the VGAM30 folded precursor RNA into VGAM30 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM30 RNA is designated SEQ ID:2741, and is provided hereinbelow with reference to the sequence listing part.

[6589] VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM30 host target RNA comprises three

regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6590] VGAM30 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM30 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM30 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target bind-

ing sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6591] The complementary binding of VGAM30 RNA, herein designated VGAM RNA, to host target binding sites on VGAM30 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM30 host target RNA into VGAM30 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6592] It is appreciated that VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM30 host target genes. The mRNA of each one of this plurality of VGAM30 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM30 RNA, herein designated VGAM RNA, and which when bound by VGAM30 RNA causes inhibition of translation of respective one or more VGAM30 host target proteins.

[6593] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM30 gene, herein designated VGAM GENE, on one or more VGAM30 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6594] It is yet further appreciated that a function of VGAM30 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM30 correlate with, and may be deduced from, the identity of the host target genes which VGAM30 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6595] Nucleotide sequences of the VGAM30 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM30 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM30 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM30 are further described hereinbelow with reference to Table 1.

[6596] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM30 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM30 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6597] As mentioned hereinabove with reference to Fig. 1, a function of VGAM30 gene, herein designated VGAM is inhibition of expression of VGAM30 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM30 correlate with, and may be deduced from, the identity of the target genes which VGAM30 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6598] Fukuyama Type Congenital Muscular Dystrophy (fukutin)

(FCMD, Accession NM_006731) is a VGAM30 host target gene. FCMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCMD BINDING SITE, designated SEQ ID:13574, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6599] A function of VGAM30 is therefore inhibition of Fukuyama Type Congenital Muscular Dystrophy (fukutin) (FCMD, Accession NM_006731). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCMD. P3 (Accession NM_019848) is another VGAM30 host target gene. P3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P3 BINDING SITE, designated SEQ ID:21254, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6600] Another function of VGAM30 is therefore inhibition of P3 (Accession NM_019848). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P3. FLJ14146 (Accession NM_024709) is another VGAM30 host target gene. FLJ14146 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14146 BINDING SITE, designated SEQ ID:24032, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6601] Another function of VGAM30 is therefore inhibition of FLJ14146 (Accession NM_024709). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14146. KIAA0935 (Accession XM_052620) is another VGAM30 host target gene. KIAA0935 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0935 BINDING SITE, designated SEQ ID:36011, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6602] Another function of VGAM30 is therefore inhibition of KIAA0935 (Accession XM_052620). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0935. P15-2 (Accession NM_018698) is another VGAM30 host target gene. P15-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P15-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P15-2 BINDING SITE, designated SEQ ID:20782, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6603] Another function of VGAM30 is therefore inhibition of P15-2 (Accession NM_018698). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P15-2.

Torsin Family 2, Member A (TOR2A, Accession NM_130459) is another VGAM30 host target gene. TOR2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOR2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOR2A BINDING SITE, designated SEQ ID:28216, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6604] Another function of VGAM30 is therefore inhibition of Torsin Family 2, Member A (TOR2A, Accession NM_130459). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOR2A. LOC144848 (Accession XM_056770) is another VGAM30 host target gene. LOC144848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144848 BINDING SITE, designated SEQ ID:36419, to the nucleotide sequence of

VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6605] Another function of VGAM30 is therefore inhibition of LOC144848 (Accession XM_056770). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144848. LOC150372 (Accession XM_086893) is another VGAM30 host target gene. LOC150372 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150372 BINDING SITE, designated SEQ ID:38940, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6606] Another function of VGAM30 is therefore inhibition of LOC150372 (Accession XM_086893). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150372. LOC163682 (Accession XM_099402) is another VGAM30 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42087, to the nucleotide sequence of VGAM30 RNA, herein designated VGAM RNA, also designated SEQ ID:2741.

[6607] Another function of VGAM30 is therefore inhibition of LOC163682 (Accession XM_099402). Accordingly, utilities of VGAM30 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163682. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 31 (VGAM31) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6608] VGAM31 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM31 was detected is described hereinabove with reference to Figs. 1–8.

[6609] VGAM31 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6610] VGAM31 gene encodes a VGAM31 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM31 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM31 precursor RNA is designated SEQ ID:17, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:17 is located at position 192106 relative to the genome of Invertebrate Iridescent Virus 6.

[6611] VGAM31 precursor RNA folds onto itself, forming VGAM31 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6612] An enzyme complex designated DICER COMPLEX, `dices` the VGAM31 folded precursor RNA into VGAM31 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM31 RNA is designated SEQ ID:2742, and is provided hereinbelow with reference to the sequence listing part.

[6613] VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM31 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6614] VGAM31 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM31 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM31 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[6615] The complementary binding of VGAM31 RNA, herein designated VGAM RNA, to host target binding sites on VGAM31 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM31 host target RNA into VGAM31 host target protein, herein design-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6616] It is appreciated that VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM31 host target genes. The mRNA of each one of this plurality of VGAM31 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM31 RNA, herein designated VGAM RNA, and which when bound by VGAM31 RNA causes inhibition of translation of respective one or more VGAM31 host target proteins.

[6617] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM31 gene, herein designated VGAM GENE, on one or more VGAM31 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6618] It is yet further appreciated that a function of VGAM31 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM31 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM31 correlate with, and may be deduced from, the identity of the host target genes which VGAM31 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6619] Nucleotide sequences of the VGAM31 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM31 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM31 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM31 are further described hereinbelow with reference to Table 1.

[6620] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM31 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM31 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6621] As mentioned hereinabove with reference to Fig. 1, a function of VGAM31 gene, herein designated VGAM is inhibition of expression of VGAM31 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM31 correlate with, and may be deduced from, the identity of the target genes which VGAM31 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6622] FLJ20209 (Accession XM_098142) is a VGAM31 host target gene. FLJ20209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20209 BINDING SITE, designated SEQ ID:41400, to the nucleotide sequence of VGAM31 RNA, herein designated VGAM RNA, also designated SEQ

ID:2742.

[6623] A function of VGAM31 is therefore inhibition of FLJ20209 (Accession XM_098142). Accordingly, utilities of VGAM31 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20209. Monocyte to Macrophage Differentiation-associated (MMD, Accession XM_008269) is another VGAM31 host target gene. MMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMD BINDING SITE, designated SEQ ID:30074, to the nucleotide sequence of VGAM31 RNA, herein designated VGAM RNA, also designated SEQ ID:2742.

[6624] Another function of VGAM31 is therefore inhibition of Monocyte to Macrophage Differentiation-associated (MMD, Accession XM_008269). Accordingly, utilities of VGAM31 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMD. LOC143920 (Accession XM_084658) is another VGAM31 host target gene. LOC143920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by LOC143920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143920 BINDING SITE, designated SEQ ID:37641, to the nucleotide sequence of VGAM31 RNA, herein designated VGAM RNA, also designated SEQ ID:2742.

[6625] Another function of VGAM31 is therefore inhibition of LOC143920 (Accession XM_084658). Accordingly, utilities of VGAM31 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143920. LOC145858 (Accession XM_085258) is another VGAM31 host target gene. LOC145858 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145858 BINDING SITE, designated SEQ ID:38002, to the nucleotide sequence of VGAM31 RNA, herein designated VGAM RNA, also designated SEQ ID:2742.

[6626] Another function of VGAM31 is therefore inhibition of LOC145858 (Accession XM_085258). Accordingly, utilities

of VGAM31 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145858. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 32 (VGAM32) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6627] VGAM32 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM32 was detected is described hereinabove with reference to Figs. 1–8.

[6628] VGAM32 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6629] VGAM32 gene encodes a VGAM32 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM32 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM32 precursor RNA is designated SEQ ID:18, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:18 is located at position 102904 relative to the genome of Invertebrate Iridescent Virus 6.

[6630] VGAM32 precursor RNA folds onto itself, forming VGAM32 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6631] An enzyme complex designated DICER COMPLEX, `dices` the VGAM32 folded precursor RNA into VGAM32 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 91%) nucleotide sequence of VGAM32 RNA is designated SEQ ID:2743, and is

provided hereinbelow with reference to the sequence listing part.

[6632] VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM32 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6633] VGAM32 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM32 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM32 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6634] The complementary binding of VGAM32 RNA, herein designated VGAM RNA, to host target binding sites on VGAM32 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM32 host target RNA into VGAM32 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6635] It is appreciated that VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM32 host target genes. The mRNA of each one of this plurality of VGAM32 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM32 RNA, herein designated VGAM

RNA, and which when bound by VGAM32 RNA causes inhibition of translation of respective one or more VGAM32 host target proteins.

[6636] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM32 gene, herein designated VGAM GENE, on one or more VGAM32 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6637] It is yet further appreciated that a function of VGAM32 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM32 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM32 correlate with, and may be deduced from, the identity of the host target genes which VGAM32 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6638] Nucleotide sequences of the VGAM32 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM32 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM32 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM32 are further described hereinbelow with reference to Table 1.

[6639] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM32 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM32 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6640] As mentioned hereinabove with reference to Fig. 1, a function of VGAM32 gene, herein designated VGAM is inhibition of expression of VGAM32 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM32 correlate with, and may be deduced from, the identity of the target genes which VGAM32 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6641] Mitogen-activated Protein Kinase Kinase Kinase 8 (MAP3K8, Accession NM_005204) is a VGAM32 host target gene. MAP3K8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K8 BINDING SITE, designated SEQ ID:11704, to the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, also designated SEQ ID:2743.

[6642] A function of VGAM32 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 8 (MAP3K8, Accession NM_005204), a gene which is able to activate $\text{nf-}\kappa\text{-b}$ 1 by stimulating proteasome-mediated p. Accordingly, utilities of VGAM32 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K8. The function of MAP3K8 has been

established by previous studies. By transfecting the hamster embryonic cell line SHOK with DNA extracted from a human thyroid carcinoma cell line, Miyoshi et al. (1991) identified the transforming oncogene 'cancer Osaka thyroid' (COT). Sequence analysis revealed that COT is a serine-threonine protein kinase. The authors compared genomic clones of COT from transformed SHOK cells and from human placenta cells and found that the COT oncogene had undergone a rearrangement within the last coding exon, an event which probably occurred during the initial transfection experiment. The COT protooncogene contains 8 exons. Aoki et al. (1993) reported that the predicted normal COT protein has 467 amino acids. In the COT oncoprotein, the C-terminal 70 amino acids of normal COT are replaced by 18 novel residues. Cell fractionation and immunoprecipitation studies demonstrated that the COT protooncogene encodes 58- and 52-kD proteins that are located in the cytosol. Both proteins have serine/threonine kinase activity. The 2 COT isoforms appear to result from the use of alternative translation initiation sites. The 58-kD isoform had stronger transforming activity than the 52-kD protein, although this activity was much weaker than that of the oncoprotein. Aoki et al.

(1993) suggested that the N-terminal domain of COT may be necessary for cellular transformation, whereas the C-terminal domain may negatively regulate the transforming activity. Chan et al. (1993) isolated a Ewing sarcoma cell line cDNA that transformed NIH3T3 cells. They designated the gene EST for 'Ewing sarcoma transformant' and identified it as COT. Since the EST cDNA encodes the normal form of the COT protein, the authors concluded that the COT gene can be activated as an oncogene by overexpression as well as by gene rearrangement. Northern blot analysis revealed that COT is expressed as a 3.2-kb mRNA in human fibroblasts and epithelial cells. Treatment of a lung fibroblast cell line with the tumor promoter okadaic acid induced COT expression

[6643] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6644] Aoki, M.; Hamada, F.; Sugimoto, T.; Sumida, S.; Akiyama, T.; Toyoshima, K. : The human cot proto-oncogene encodes two protein serine/threonine kinases with different transforming activities by alternative initiation of translation. J. Biol. Chem. 268: 22723-22732, 1993. ; and

[6645] Chan, A. M.-L.; Chedid, M.; McGovern, E. S.; Popescu, N.

C.; Miki, T.; Aaronson, S. A. : Expression cDNA cloning of a serine kinase transforming gene. *Oncogene* 8: 1329–1333, 1993.

[6646] Further studies establishing the function and utilities of MAP3K8 are found in John Hopkins OMIM database record ID 603259, and in cited publications numbered 850 and 9052–8738 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1795 (Accession XM_050988) is another VGAM32 host target gene. KIAA1795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1795 BINDING SITE, designated SEQ ID:35698, to the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, also designated SEQ ID:2743.

[6647] Another function of VGAM32 is therefore inhibition of KIAA1795 (Accession XM_050988). Accordingly, utilities of VGAM32 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1795. LOC143666 (Accession XM_096465) is another

VGAM32 host target gene. LOC143666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143666 BINDING SITE, designated SEQ ID:40368, to the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, also designated SEQ ID:2743.

[6648] Another function of VGAM32 is therefore inhibition of LOC143666 (Accession XM_096465). Accordingly, utilities of VGAM32 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143666. LOC253258 (Accession XM_172870) is another VGAM32 host target gene. LOC253258 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253258, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253258 BINDING SITE, designated SEQ ID:46146, to the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, also designated SEQ ID:2743.

[6649] Another function of VGAM32 is therefore inhibition of LOC253258 (Accession XM_172870). Accordingly, utilities of VGAM32 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253258. LOC96573 (Accession XM_032391) is another VGAM32 host target gene. LOC96573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC96573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96573 BINDING SITE, designated SEQ ID:31642, to the nucleotide sequence of VGAM32 RNA, herein designated VGAM RNA, also designated SEQ ID:2743.

[6650] Another function of VGAM32 is therefore inhibition of LOC96573 (Accession XM_032391). Accordingly, utilities of VGAM32 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96573. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 33 (VGAM33) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[6651] VGAM33 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM33 was detected is described hereinabove with reference to Figs. 1–8.

[6652] VGAM33 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6653] VGAM33 gene encodes a VGAM33 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM33 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM33 precursor RNA is designated SEQ ID:19, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:19 is located at position 72913 relative to the genome of Invertebrate Iridescent Virus 6.

[6654] VGAM33 precursor RNA folds onto itself, forming VGAM33 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6655] An enzyme complex designated DICER COMPLEX, `dices` the VGAM33 folded precursor RNA into VGAM33 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM33 RNA is designated SEQ ID:2744, and is provided hereinbelow with reference to the sequence listing part.

[6656] VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM33 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6657] VGAM33 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM33 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM33 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[6658] The complementary binding of VGAM33 RNA, herein designated VGAM RNA, to host target binding sites on VGAM33 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM33 host target RNA into VGAM33 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6659] It is appreciated that VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM33 host target genes. The mRNA of each one of this plurality of VGAM33 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM33 RNA, herein designated VGAM RNA, and which when bound by VGAM33 RNA causes inhibition of translation of respective one or more VGAM33 host target proteins.

[6660] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM33 gene, herein designated VGAM GENE, on one or

more VGAM33 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6661] It is yet further appreciated that a function of VGAM33 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM33 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM33 correlate with, and may be deduced from, the identity of the host target genes which VGAM33 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6662] Nucleotide sequences of the VGAM33 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM33 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM33 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM33 are further de-
scribed hereinbelow with reference to Table 1.

[6663] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM33 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM33 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[6664] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM33 gene, herein designated VGAM is in-
hibition of expression of VGAM33 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM33 correlate with, and may be deduced from, the
identity of the target genes which VGAM33 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[6665] Protocadherin 10 (PCDH10, Accession NM_020815) is a
VGAM33 host target gene. PCDH10 BINDING SITE1 and

PCDH10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2, designated SEQ ID:21881 and SEQ ID:26765 respectively, to the nucleotide sequence of VGAM33 RNA, herein designated VGAM RNA, also designated SEQ ID:2744.

[6666] A function of VGAM33 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM_020815). Accordingly, utilities of VGAM33 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 34 (VGAM34) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6667] VGAM34 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM34 was detected is described hereinabove with reference to Figs. 1–8.

[6668] VGAM34 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6669] VGAM34 gene encodes a VGAM34 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM34 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM34 precursor RNA is designated SEQ ID:20, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:20 is located at position 157322 relative to the genome of Invertebrate Iridescent Virus 6.

[6670] VGAM34 precursor RNA folds onto itself, forming VGAM34 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first

half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6671] An enzyme complex designated DICER COMPLEX, `dices` the VGAM34 folded precursor RNA into VGAM34 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM34 RNA is designated SEQ ID:2745, and is provided hereinbelow with reference to the sequence listing part.

[6672] VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM34 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6673] VGAM34 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM34 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM34 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM34 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6674] The complementary binding of VGAM34 RNA, herein designated VGAM RNA, to host target binding sites on VGAM34 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM34 host target RNA into VGAM34 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6675] It is appreciated that VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM34 host target genes. The mRNA of each one of this plurality of VGAM34 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM34 RNA, herein designated VGAM RNA, and which when bound by VGAM34 RNA causes inhibition of translation of respective one or more VGAM34 host target proteins.

[6676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM34 gene, herein designated VGAM GENE, on one or more VGAM34 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6677] It is yet further appreciated that a function of VGAM34 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM34 correlate with, and may be deduced from, the identity of the host target genes which VGAM34 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6678] Nucleotide sequences of the VGAM34 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM34 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM34 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM34 are further described hereinbelow with reference to Table 1.

[6679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM34 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM34 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6680] As mentioned hereinabove with reference to Fig. 1, a function of VGAM34 gene, herein designated VGAM is inhibition of expression of VGAM34 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM34 correlate with, and may be deduced from, the identity of the target genes which VGAM34 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6681] Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM_003678) is a VGAM34 host target gene. C22orf19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of C22orf19 BINDING SITE, designated SEQ ID:9777, to the nucleotide sequence of VGAM34 RNA, herein designated VGAM RNA, also designated SEQ ID:2745.

[6682] A function of VGAM34 is therefore inhibition of Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM_003678). Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf19. FLJ10545 (Accession NM_018132) is another VGAM34 host target gene.

FLJ10545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10545 BINDING SITE, designated SEQ ID:19930, to the nucleotide sequence of VGAM34 RNA, herein designated VGAM RNA, also designated SEQ ID:2745.

[6683] Another function of VGAM34 is therefore inhibition of FLJ10545 (Accession NM_018132). Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ10545. Protocadherin 20 (PCDH20, Accession NM_022843) is another VGAM34 host target gene. PCDH20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH20 BINDING SITE, designated SEQ ID:23138, to the nucleotide sequence of VGAM34 RNA, herein designated VGAM RNA, also designated SEQ ID:2745.

[6684] Another function of VGAM34 is therefore inhibition of Protocadherin 20 (PCDH20, Accession NM_022843). Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH20. LOC144866 (Accession XM_096699) is another VGAM34 host target gene. LOC144866 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144866, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144866 BINDING SITE, desig-

nated SEQ ID:40480, to the nucleotide sequence of VGAM34 RNA, herein designated VGAM RNA, also designated SEQ ID:2745.

[6685] Another function of VGAM34 is therefore inhibition of LOC144866 (Accession XM_096699). Accordingly, utilities of VGAM34 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144866. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 35 (VGAM35) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6686] VGAM35 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM35 was detected is described hereinabove with reference to Figs. 1–8.

[6687] VGAM35 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6688] VGAM35 gene encodes a VGAM35 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM35 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM35 precursor RNA is designated SEQ ID:21, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:21 is located at position 109599 relative to the genome of Invertebrate Iridescent Virus 6.

[6689] VGAM35 precursor RNA folds onto itself, forming VGAM35 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6690] An enzyme complex designated DICER COMPLEX, `dices` the VGAM35 folded precursor RNA into VGAM35 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM35 RNA is designated SEQ ID:2746, and is provided hereinbelow with reference to the sequence listing part.

[6691] VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM35 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6692] VGAM35 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM35 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration,

Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM35 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6693] The complementary binding of VGAM35 RNA, herein designated VGAM RNA, to host target binding sites on VGAM35 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM35 host target RNA into VGAM35 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6694] It is appreciated that VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM35 host target genes. The mRNA of each one of this plurality of VGAM35 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM35 RNA, herein designated VGAM RNA, and which when bound by VGAM35 RNA causes inhibition of translation of respective one or more VGAM35 host target proteins.

[6695] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM35 gene, herein designated VGAM GENE, on one or more VGAM35 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective:

Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6696] It is yet further appreciated that a function of VGAM35 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM35 correlate with, and may be deduced from, the identity of the host target genes which VGAM35 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6697] Nucleotide sequences of the VGAM35 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM35 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM35 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM35 are further described hereinbelow with reference to Table 1.

[6698] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM35 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM35 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[6699] As mentioned hereinabove with reference to Fig. 1, a function of VGAM35 gene, herein designated VGAM is inhibition of expression of VGAM35 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM35 correlate with, and may be deduced from, the identity of the target genes which VGAM35 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6700] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 5 (aggrecanase-2) (ADAMTS5, Accession NM_007038) is a VGAM35 host target gene. ADAMTS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS5 BINDING SITE, designated SEQ ID:13919, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6701] A function of VGAM35 is therefore inhibition of A Disinte-

grin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 5 (aggrecanase-2) (ADAMTS5, Accession NM_007038), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS5. The function of ADAMTS5 has been established by previous studies. Proteolysis of the extracellular matrix plays a critical role in establishing tissue architecture during development and in tissue degradation in diseases such as cancer, arthritis, Alzheimer disease, and a variety of inflammatory conditions. The proteolytic enzymes responsible include members of diverse protease families and they may work in concert or in cascades to degrade or process molecules. Two groups of zinc metalloproteinases in particular, ADAMs and MMPs (e.g., 600754), appear broadly relevant to extracellular proteolysis. Most ADAM family members are quite similar in domain organization, bearing, from amino to carboxyl termini, a signal peptide, a proregion, a zinc metalloprotease catalytic domain with the typical reprolysin signature motif, a disintegrin domain, a cysteine-rich domain, an EGF-like domain, and, in many cases, a

membrane-spanning region and a cytoplasmic domain with signaling potential. Members of the ADAMTS family differ substantially from the prototypic ADAM structure in that they lack the EGF-like domain, do not have a canonical disintegrin sequence, and possess modules with similar thrombospondin type 1 repeats. By searching an EST database using the protein sequences of human ADAMTS1 to ADAMTS4 and a *C. elegans* ADAMTS as queries, Hurskainen et al. (1999) identified ADAMTS5, ADAMTS6 (OMIM Ref. No. 605008), and ADAMTS7 (OMIM Ref. No. 605009). They determined a partial human ADAMTS5 cDNA sequence that lacked 5-prime coding sequence. The predicted partial ADAMTS5 protein has the domain structure characteristic of ADAMTSs, beginning with a partial metalloproteinase domain. Northern blot analysis of several human tissues detected an approximately 10-kb ADAMTS5 transcript that was expressed at a low level in placenta and at barely detectable levels in a number of other tissues. Northern blot analysis showed that mouse Adamts5 was specifically expressed in a 7-day mouse embryo, and at low or undetectable levels thereafter. In situ hybridization of an 8.5-day mouse embryo showed uniform Adamts5 expression throughout the embryo. In

addition, Adamts5 expression was found in trophoblastic cells lining the uterine cavity, in the developing placenta, and in the decidual reaction within the uterus. In a 10.5-day mouse embryo, Adamts5 expression was widespread, but at a lower level than in the 8.5-day embryo. Expression was found in mesenchyme and somites, as well as in the neural tube and developing hindgut. Abbaszade et al. (1999) demonstrated that recombinant ADAMTS5 expressed in insect cells cleaves aggrecan at the glu373-ala374 site, with the cleavage pattern and inhibitor profile indistinguishable from that observed with native aggrecanase. Northern blot analysis of several human tissues showed highest ADAMTS5 expression in placenta, with much lower expression in heart and brain. Major transcripts of 12.4, 10.7, 8.6, and 6.6 kb were detected. Real time PCR of a number of normal human tissues detected ADAMTS5 expression in placenta, cervix, uterus, bladder, and esophagus. Expression was also found in rib cartilage, chondroblastoma, and fibrous tissue and joint capsule samples from an arthritic patient.

[6702] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [6703] Abbaszade, I.; Liu, R.-Q.; Yang, F.; Rosenfeld, S. A.; Ross, O. H.; Link, J. R.; Ellis, D. M.; Tortorella, M. D.; Pratta, M. A.; Hollis, J. M.; Wynn, R.; Duke, J. L.; and 15 others : Cloning and characterization of ADAMTS11, an aggrecanase from the ADAMTS family. *J. Biol. Chem.* 274: 23443–23450, 1999. ; and
- [6704] Hurskainen, T. L.; Hirohata, S.; Seldin, M. F.; Apte, S. S. : ADAM-TS5, ADAM-TS6, and ADAM-TS7, novel members of a new family of zinc metalloproteases: general features and genomic dis.
- [6705] Further studies establishing the function and utilities of ADAMTS5 are found in John Hopkins OMIM database record ID 605007, and in cited publications numbered 291 and 7604 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hephaestin (HEPH, Accession NM_014799) is another VGAM35 host target gene. HEPH BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HEPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEPH BINDING SITE, designated SEQ ID:16717, to the nucleotide sequence of

VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6706] Another function of VGAM35 is therefore inhibition of Hephaestin (HEPH, Accession NM_014799), a gene which is thought to be a membrane-bound protein responsible for transport of dietary iron from epithelial cells of the intestinal lumen into the circulatory system. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEPH. The function of HEPH has been established by previous studies. Vulpe et al. (1999) found that Heph expression contrasts that of Cp, which is highly expressed in liver and expressed to a lesser extent in other tissues, including brain and lung, but is not expressed in intestine, where the highest expression of Heph is found. In situ hybridization studies indicated that intestinal expression of Heph is limited to villi, with almost no signal observed in crypt cells. Iron absorption occurs in villi. Vulpe et al. (1999) found that sla mice have a deletion of 582 nucleotides from the Heph gene, predicting an in-frame omission of 194 amino acids in the gene product. On the basis of its homology with ceruloplasmin, Vulpe et al. (1999) proposed that hephaestin is a ferroxidase neces-

sary for iron release from intestinal epithelial cells. Since it contains only 1 putative membrane-spanning domain, it is unlikely to be a transmembrane iron carrier itself; hephaestin may interact with an iron-transport protein to facilitate the movement of iron across the membrane. Heph-
haestin represents a link between copper and iron metabolism in mammals and offers a basis for the iron-deficiency anemia associated with copper deficiency. Copper deficiency results in the decreased absorption of dietary iron, which enters intestinal epithelium normally but cannot exit into the circulation. Indeed, intestinal iron accumulation in copper-deficient swine is similar to the iron accumulation seen in sla mice (Lee et al., 1968). The administration of copper, but not iron, to copper-deficient pigs alleviates the anemia and facilitates the egress of iron from tissues, including intestine.

[6707] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6708] Vulpe, C. D.; Kuo, Y.-M.; Murphy, T. L.; Cowley, L.; Askwith, C.; Libina, N.; Gitschier, J.; Anderson, G. J. : Heph-
haestin, a ceruloplasmin homologue implicated in intestinal iron transport, is defective in the sla mouse. Nature

Genet. 21: 195–199, 1999. ; and

[6709] Lee, G. R.; Nacht, S.; Lukens, J. N.; Cartwright, G. E. : Iron metabolism in copper-deficient swine. J. Clin. Invest. 47: 2058–2069, 1968.

[6710] Further studies establishing the function and utilities of HEPH are found in John Hopkins OMIM database record ID 300167, and in cited publications numbered 7244–7250 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lipin 1 (LPIN1, Accession XM_041136) is another VGAM35 host target gene. LPIN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LPIN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN1 BINDING SITE, designated SEQ ID:33471, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6711] Another function of VGAM35 is therefore inhibition of Lipin 1 (LPIN1, Accession XM_041136), a gene which is involved in adipocyte differentiation (by similarity). Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with LPIN1. The function of LPIN1 has been established by previous studies. Mice carrying mutations in the fatty liver dystrophy (fld) gene have features of human lipodystrophy (Reue et al., 2000). In the human, lipodystrophy is a heterogeneous group of disorders characterized by loss of body fat, fatty liver, hypertriglyceridemia, and insulin resistance. Through positional cloning, Peterfy et al. (2001) isolated the gene responsible for fatty liver dystrophy in mice and characterized 2 independent mutant alleles of the fld gene. They designated the gene *Lpin1* and named the novel nuclear protein which it encodes lipin. Through database searches, Peterfy et al. (2001) identified several mouse and human EST and genomic sequences with similarities to *Lpin1*. These included 2 *Lpin1*-related mouse genes (*Lpin2* and *Lpin3*) and 3 human homologs (LPIN1, LPIN2 (OMIM Ref. No. 605519), and LPIN3 (OMIM Ref. No. 605520)). LPIN1 is identical to the KIAA0188 gene identified by Nagase et al. (1996). Consistent with the observed reduction of adipose tissue mass in fld mice, wildtype *Lpin1* mRNA was expressed at high levels in adipose tissue and was induced during differentiation of 3T3-L1 preadipocytes. The results indicated that lipin is required for normal adipose

tissue development, and provided a candidate gene for human lipodystrophy Cao and Hegele (2002) sequenced the 21 exons of the LPIN1 gene in lipodystrophy patients who had no mutations in known lipodystrophy genes, and also in normal control subjects. They found no rare LPIN1 coding sequence variants that were exclusive to patients with lipodystrophy. However, they found 4 single nucleotide polymorphisms (SNPs).

[6712] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6713] Reue, K.; Xu, P.; Wang, X.-P.; Slavin, B. G. : Adipose tissue deficiency, glucose intolerance, and increased atherosclerosis result from mutation in the mouse fatty liver dystrophy (fld) gene. J. Lipid Res. 41: 1067–1076, 2000. ; and

[6714] Cao, H.; Hegele, R. A. : Identification of single-nucleotide polymorphisms in the human LPIN1 gene. J. Hum. Genet. 47: 370–372, 2002.

[6715] Further studies establishing the function and utilities of LPIN1 are found in John Hopkins OMIM database record ID 605518, and in cited publications numbered 645 and 11385–6461 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence.RAB7, Member RAS Oncogene Family (RAB7, Accession NM_004637) is another VGAM35 host target gene. RAB7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB7 BINDING SITE, designated SEQ ID:11013, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6716] Another function of VGAM35 is therefore inhibition of RAB7, Member RAS Oncogene Family (RAB7, Accession NM_004637), a gene which is an important regulator of vesicular transport in the late endocytic pathway. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB7. The function of RAB7 has been established by previous studies. Members of the RAB family of RAS-related GTP-binding proteins are important regulators of vesicular transport and are located in specific intracellular compartments. RAB7 has been localized to late endosomes and shown to be important in the late endocytic pathway. In addition, it has been shown to have a

fundamental role in the cellular vacuolation induced by the cytotoxin VacA of *Helicobacter pylori*. Vitelli et al. (1996) cloned a RAB7 cDNA by screening a human placenta cDNA library with a rat Rab7 cDNA. The RAB7 cDNA encodes a 207-amino acid protein whose sequence is 99% identical to those of mouse, rat, and dog Rab7 and 61% identical to that of yeast Rab7. Using Northern blot analysis, Vitelli et al. (1996) found that RAB7 was expressed as 1.7- and 2.5-kb transcripts in all cell lines examined but that there was a large difference in the total amount of RAB7 mRNA among the cell lines. In studies using anti-sense RNA, Davies et al. (1997) found that downregulation of RAB7 gene expression in HeLa cells using antisense RNA induces severe cell vacuolation that resembles the phenotype seen in fibroblasts from patients with Chediak-Higashi syndrome (OMIM Ref. No. 214500). Davies et al. (1997) mapped the RAB7 gene to chromosome 3 by PCR analysis of somatic cell hybrid DNAs. Barbosa et al. (1995) mapped the mouse Rab7 gene to chromosome 9 by intersubspecific backcross analysis. Using fluorescence in situ hybridization and somatic cell hybrid analysis, Kashuba et al. (1997) mapped the RAB7 gene to 3q21.

[6717] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [6718] Davies, J. P.; Cotter, P. D.; Ioannou, Y. A. : Cloning and mapping of human Rab7 and Rab9 cDNA sequences and identification of a Rab9 pseudogene. *Genomics* 41: 131–134, 1997. ; and
- [6719] Davies, J. P.; Cotter, P. D.; Ioannou, Y. A. : Cloning and mapping of human Rab7 and Rab9 cDNA sequences and identification of a Rab9 pseudogene. *Genomics* 41: 131–134, 1997.
- [6720] Further studies establishing the function and utilities of RAB7 are found in John Hopkins OMIM database record ID 602298, and in cited publications numbered 544 and 10997 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Reelin (RELN, Accession XM_168628) is another VGAM35 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45284, to the nucleotide sequence of VGAM35 RNA,

herein designated VGAM RNA, also designated SEQ ID:2746.

[6721] Another function of VGAM35 is therefore inhibition of Reelin (RELN, Accession XM_168628), a gene which regulates microtubule function in neurons and neuronal migration. Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN has been established by previous studies. Normal development of the cerebral cortex requires long-range migration of cortical neurons from proliferative regions deep in the brain. Lissencephaly ('smooth brain,' from 'lissos,' meaning 'smooth,' and 'encephalos,' meaning 'brain') is a severe developmental disorder in which neuronal migration is impaired, leading to a thickened cerebral cortex whose normally folded contour is simplified and smooth. X-linked lissencephaly (OMIM Ref. No. 300067) is caused by mutation in the gene encoding doublecortin (DCX; 300121). Deletion of or mutation in the LIS1 gene (OMIM Ref. No. 601545), located on 17p, causes isolated lissencephaly sequence (ILS), and haploinsufficiency of this and other neighboring genes is responsible for the Miller-Dieker lissencephaly syndrome (OMIM Ref. No.

247200), a contiguous gene deletion syndrome.

Lissencephaly is a feature of a number of syndromes, such as the Walker–Warburg syndrome (OMIM Ref. No.

236670). Hong et al. (2000) studied an autosomal recessive form of lissencephaly associated with severe abnormalities of the cerebellum, hippocampus, and brainstem; see lissencephaly syndrome, Norman–Roberts type (OMIM Ref. No. 257320). They tested for linkage to markers near RELN on chromosome 7 and DAB1 on 1p32–p31, because mutations in the mouse homologs of these 2 genes cause brain defects in mice that resemble lissencephaly, including hypoplasia of the cerebellum, brainstem abnormalities, and a neuronal migration disorder of the neocortex and hippocampus. In 2 unrelated pedigrees, they found substantial regions of homozygosity in affected children near the RELN locus on 7q22. In these 2 families, they demonstrated different splice site mutations in the RELN gene. The study of these human patients pointed to several previously unsuspected functions of reelin in and outside of the brain. Although abnormalities of RELN mRNA had been reported in postmortem brains of schizophrenic humans (Impagnatiello et al., 1998), no evidence of schizophrenia was found in individuals with het–

erozygous or homozygous RELN mutations. On the other hand, one of the lissencephaly patients studied with a muscle biopsy showed evidence of abnormal neuromuscular connectivity (Hourihane et al., 1993). Moreover, at least 3 patients had persistent lymphedema neonatally, and one showed accumulation of chylous (i.e., fatty) ascites fluid that required peritoneal shunting (Hourihane et al., 1993). The apparent role for reelin in serum homeostasis may reflect reelin interactions with LDL superfamily receptors outside the brain, as well as in the brain. Animal model experiments lend further support to the function of RELN. To investigate Reln function, Magdaleno et al. (2002) generated transgenic mice using the nestin (NES; 600915) promoter to drive ectopic expression of Reln in the ventricular zone during early brain development. Ectopic Reln expression in transgenic reelin mice, which lack endogenous Reln expression, induced tryosine phosphorylation of Dab1 in the ventricular zone. The transgene also rescued some, but not all, of the neuroanatomic and behavioral abnormalities characteristic of the reeler phenotype, including ataxia and the migration of Purkinje cells. Magdaleno et al. (2002) hypothesized that Reln functions in concert with other positional cues to

promote cell–cell interactions that are required for layer formation during development.

[6722] It is appreciated that the abovementioned animal model for RELN is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6723] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6724] Hong, S. E.; Shugart, Y. Y.; Huang, D. T.; Al Shahwan, S.; Grant, P. E.; Hourihane, J. O.; Martin, N. D. T.; Walsh, C. A. : Autosomal recessive lissencephaly with cerebellar hypoplasia is associated with human RELN mutations. *Nature Genet.* 26: 93–96, 2000. Note: Erratum: *Nature Genet.* 27: 225 only, 2001. ; and

[6725] Magdaleno, S.; Keshvara, L.; Curran, T. : Rescue of ataxia and preplate splitting by ectopic expression of reelin in reeler mice. *Neuron* 33: 573–586, 2002.

[6726] Further studies establishing the function and utilities of RELN are found in John Hopkins OMIM database record ID 600514, and in cited publications numbered 7209–7214, 10019–722 and 10024 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence. Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM_000452) is another VGAM35 host target gene. SLC10A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC10A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC10A2 BINDING SITE, designated SEQ ID:6067, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6727] Another function of VGAM35 is therefore inhibition of Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM_000452). Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC10A2. Coactosin-like 1 (Dictyostelium) (COTL1, Accession XM_113840) is another VGAM35 host target gene. COTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of COTL1 BINDING SITE, designated SEQ ID:42469, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6728] Another function of VGAM35 is therefore inhibition of Coactosin-like 1 (Dictyostelium) (COTL1, Accession XM_113840). Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COTL1. KIAA0326 (Accession XM_034819) is another VGAM35 host target gene.

KIAA0326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0326 BINDING SITE, designated SEQ ID:32156, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6729] Another function of VGAM35 is therefore inhibition of KIAA0326 (Accession XM_034819). Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0326. LOC255328 (Accession XM_172920) is another VGAM35 host target gene. LOC255328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255328 BINDING SITE, designated SEQ ID:46182, to the nucleotide sequence of VGAM35 RNA, herein designated VGAM RNA, also designated SEQ ID:2746.

[6730] Another function of VGAM35 is therefore inhibition of LOC255328 (Accession XM_172920). Accordingly, utilities of VGAM35 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255328. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 36 (VGAM36) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6731] VGAM36 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM36 was detected is described hereinabove with reference to Figs. 1–8.

[6732] VGAM36 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6733] VGAM36 gene encodes a VGAM36 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM36 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM36 precursor RNA is designated SEQ ID:22, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:22 is located at position 14270 relative to the genome of Invertebrate Iridescent Virus 6.

[6734] VGAM36 precursor RNA folds onto itself, forming VGAM36 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is

due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6735] An enzyme complex designated DICER COMPLEX, `dices` the VGAM36 folded precursor RNA into VGAM36 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 92%) nucleotide sequence of VGAM36 RNA is designated SEQ ID:2747, and is provided hereinbelow with reference to the sequence listing part.

[6736] VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM36 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6737] VGAM36 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM36 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM36 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6738] The complementary binding of VGAM36 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM36 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM36 host target RNA into VGAM36 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6739] It is appreciated that VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM36 host target genes. The mRNA of each one of this plurality of VGAM36 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM36 RNA, herein designated VGAM RNA, and which when bound by VGAM36 RNA causes inhibition of translation of respective one or more VGAM36 host target proteins.

[6740] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM36 gene, herein designated VGAM GENE, on one or more VGAM36 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6741] It is yet further appreciated that a function of VGAM36 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM36 correlate with, and may be deduced from, the identity of the host target genes which VGAM36 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6742] Nucleotide sequences of the VGAM36 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM36 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM36 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM36 are further described hereinbelow with reference to Table 1.

[6743] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM36 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM36 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6744] As mentioned hereinabove with reference to Fig. 1, a function of VGAM36 gene, herein designated VGAM is inhibition of expression of VGAM36 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM36 correlate with, and may be deduced from, the identity of the target genes which VGAM36 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6745] Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043) is a VGAM36 host target gene. SLC6A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A6, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A6 BINDING SITE, designated SEQ ID:9004, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6746] A function of VGAM36 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043), a gene which transports taurine and other beta-amino acids like beta-alanine. Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A6. The function of SLC6A6 has been established by previous studies. Taurine (2-aminoethanesulfonic acid) is a major intracellular amino acid in mammals. It is involved in a number of important physiologic processes, including bile acid conjugation in hepatocytes, modulation of calcium flux and neural excitability, osmoregulation, detoxification, and membrane stabilization. The cells of most organisms respond to hypertonicity by the intracellular accumulation of high concentrations of small organic solutes (osmolytes) that, in contrast to high concentrations of electrolytes, do

not perturb the function of macromolecules. The renal medulla is normally the only tissue in mammals that undergoes wide shifts in tonicity. Its hypertonicity when the kidney is excreting a concentrated urine is fundamental to water conservation. The taurine content of the renal medulla of rats infused with 5% NaCl is higher than that in controls, suggesting that taurine behaves as an osmolyte in the renal medulla. Indeed, taurine functions as an osmolyte in Madin–Darby canine kidney (MDCK) cells. When MDCK cells cultured in isotonic medium are switched to hypertonic medium, their content of taurine doubles through the taking up of taurine from the medium. Taurine transport in these cells is dependent on sodium and chloride ions and is localized primarily in the basolateral plasma membrane. Uchida et al. (1992) cloned the cDNA for the taurine transporter in MDCK cells. The sequence of the cDNA indicated that the taurine transporter has considerable amino acid sequence similarity to previously cloned Na(+)- and Cl(-)-dependent transporters. Northern hybridization indicated that the quantity of mRNA for the taurine transporter in MDCK cells is regulated by hypertonicity. Furthermore, the Northern hybridizations indicated that the taurine transporter is present also in ileal

mucosa, brain, liver, and heart.

[6747] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6748] Ramamoorthy, S.; Leibach, F. H.; Mahesh, V. B.; Han, H.; Yang-Feng, T.; Blakely, R. D.; Ganapathy, V. : Functional characterization and chromosomal localization of a cloned taurine transporter from human placenta. *Biochem. J.* 300: 893–900, 1994. ; and

[6749] Uchida, S.; Kwon, H. M.; Yamauchi, A.; Preston, A. S.; Marumo, F.; Handler, J. S. : Molecular cloning of the cDNA for an MDCK cell Na(+)- and Cl(-)-dependent taurine transporter that is r.

[6750] Further studies establishing the function and utilities of SLC6A6 are found in John Hopkins OMIM database record ID 186854, and in cited publications numbered 5710–571 and 5776 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SMURF1 (Accession XM_166483) is another VGAM36 host target gene. SMURF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMURF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SMURF1 BINDING SITE, designated SEQ ID:44410, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6751] Another function of VGAM36 is therefore inhibition of SMURF1 (Accession XM_166483). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMURF1. TEM7 (Accession NM_020405) is another VGAM36 host target gene. TEM7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM7 BINDING SITE, designated SEQ ID:21668, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6752] Another function of VGAM36 is therefore inhibition of TEM7 (Accession NM_020405), a gene which involves in angiogenesis. Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with TEM7. The function of TEM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM23. Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394) is another VGAM36 host target gene. ZNF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF10 BINDING SITE, designated SEQ ID:17693, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6753] Another function of VGAM36 is therefore inhibition of Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394), a gene which may function as a transcriptional regulator. Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF10. The function of ZNF10 has been established by previous studies. In the course of mapping 27 nonoverlapping zinc finger cDNAs from human T cells by analysis of somatic cell hybrids, Huebner et al. (1991)

mapped zinc finger protein-10 (KOX1) to 12q13-qter, probably clustered with zinc finger protein-26 (OMIM Ref. No. 194537). Rousseau-Merck et al. (1993) also mapped the KOX1 (ZNF10) gene to 12q24.33 and demonstrated that it and KOX20 (ZNF26) are located within a pulsed field gel electrophoresis fragment less than 300 kb long. The mapping was done by a combination of somatic cell hybridization and in situ hybridization. Since ZNF26 has been mapped to 12q24.33 by in situ hybridization, this also must be the localization of ZNF10.

[6754] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6755] Huebner, K.; Druck, T.; Croce, C. M.; Thiesen, H. J. : Twenty-seven nonoverlapping zinc finger cDNAs from human T cells map to nine different chromosomes with apparent clustering. *Am. J. Hum. Genet.* 48: 726-740, 1991. ; and

[6756] Rousseau-Merck, M.-F.; Hillion, J.; Jonveaux, P.; Couillin, P.; Seite, P.; Thiesen, H.-J.; Berger, R. : Chromosomal localization of 9 KOX zinc finger genes: physical linkages suggest cluste.

[6757] Further studies establishing the function and utilities of

ZNF10 are found in John Hopkins OMIM database record ID 194538, and in cited publications numbered 10025–10026 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp547H025 (Accession NM_020161) is another VGAM36 host target gene. DKFZp547H025 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp547H025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547H025 BINDING SITE, designated SEQ ID:21371, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6758] Another function of VGAM36 is therefore inhibition of DKFZp547H025 (Accession NM_020161). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547H025. FLJ12704 (Accession NM_024998) is another VGAM36 host target gene. FLJ12704 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12704 BINDING SITE, designated SEQ ID:24561, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6759] Another function of VGAM36 is therefore inhibition of FLJ12704 (Accession NM_024998). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12704. KDEL (Lys-Asp-Glu-Leu) Endoplasmic Reticulum Protein Retention Receptor 3 (KDEL3, Accession NM_006855) is another VGAM36 host target gene. KDEL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KDEL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KDEL3 BINDING SITE, designated SEQ ID:13723, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6760] Another function of VGAM36 is therefore inhibition of KDEL (Lys-Asp-Glu-Leu) Endoplasmic Reticulum Protein Retention Receptor 3 (KDEL3, Accession NM_006855).

Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KDELR3. KIAA1817 (Accession XM_042978) is another VGAM36 host target gene.

KIAA1817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1817 BINDING SITE, designated SEQ ID:33859, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6761] Another function of VGAM36 is therefore inhibition of KIAA1817 (Accession XM_042978). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1817. LOC153727 (Accession XM_098422) is another VGAM36 host target gene. LOC153727 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC153727 BINDING SITE, designated SEQ ID:41679, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6762] Another function of VGAM36 is therefore inhibition of LOC153727 (Accession XM_098422). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153727. LOC158382 (Accession XM_098931) is another VGAM36 host target gene. LOC158382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158382 BINDING SITE, designated SEQ ID:41962, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6763] Another function of VGAM36 is therefore inhibition of LOC158382 (Accession XM_098931). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158382. LOC196264 (Accession XM_113683) is an-

other VGAM36 host target gene. LOC196264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196264 BINDING SITE, designated SEQ ID:42336, to the nucleotide sequence of VGAM36 RNA, herein designated VGAM RNA, also designated SEQ ID:2747.

[6764] Another function of VGAM36 is therefore inhibition of LOC196264 (Accession XM_113683). Accordingly, utilities of VGAM36 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196264. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 37 (VGAM37) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6765] VGAM37 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM37 was detected is described

hereinabove with reference to Figs. 1–8.

[6766] VGAM37 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6767] VGAM37 gene encodes a VGAM37 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM37 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM37 precursor RNA is designated SEQ ID:23, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:23 is located at position 141488 relative to the genome of Invertebrate Iridescent Virus 6.

[6768] VGAM37 precursor RNA folds onto itself, forming VGAM37 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate

or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6769] An enzyme complex designated DICER COMPLEX, `dices` the VGAM37 folded precursor RNA into VGAM37 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM37 RNA is designated SEQ ID:2748, and is provided hereinbelow with reference to the sequence listing part.

[6770] VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM37 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6771] VGAM37 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM37 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM37 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6772] The complementary binding of VGAM37 RNA, herein designated VGAM RNA, to host target binding sites on VGAM37 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM37 host target RNA into VGAM37 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6773] It is appreciated that VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM37 host target genes. The mRNA of each one of this plurality of VGAM37 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM37 RNA, herein designated VGAM RNA, and which when bound by VGAM37 RNA causes inhibition of translation of respective one or more VGAM37 host target proteins.

[6774] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM37 gene, herein designated VGAM GENE, on one or more VGAM37 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only

for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6775] It is yet further appreciated that a function of VGAM37 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM37 correlate with, and may be deduced from, the identity of the host target genes which VGAM37 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6776] Nucleotide sequences of the VGAM37 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM37 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM37 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM37 are further de-

scribed hereinbelow with reference to Table 1.

[6777] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM37 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM37 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6778] As mentioned hereinabove with reference to Fig. 1, a function of VGAM37 gene, herein designated VGAM is inhibition of expression of VGAM37 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM37 correlate with, and may be deduced from, the identity of the target genes which VGAM37 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6779] Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM_020390) is a VGAM37 host target gene. EIF5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of EIF5A2 BINDING SITE, designated SEQ ID:21661, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6780] A function of VGAM37 is therefore inhibition of Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM_020390). Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5A2. Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM_022549) is another VGAM37 host target gene. FEZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEZ1 BINDING SITE, designated SEQ ID:22875, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6781] Another function of VGAM37 is therefore inhibition of Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM_022549), a gene which Zygin 1; may have a role in axonal outgrowth; has similarity to C. elegans

UNC-76. Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEZ1. The function of FEZ1 has been established by previous studies. Ishii et al. (1999) positionally cloned and characterized the FEZ1/LZTS1 (leucine zipper, putative tumor suppressor-1) gene at 8p22, a region that is lost in many tumors, including prostate, breast, head and neck, esophageal, and urinary bladder carcinomas. The predicted FEZ1 protein contained a leucine-zipper region with similarity to the DNA-binding domain of the cAMP-responsive activating transcription factor-5 (OMIM Ref. No. 606398). Northern blot analysis revealed that FEZ2 is expressed almost ubiquitously in normal tissues, although expression is most abundant in testes. FEZ1 expression was undetectable in more than 60% of epithelial tumors, but FEZ1 mutations were found in primary esophageal cancers and in a prostate cancer cell line. Transcript analysis from several FEZ1-expressing tumors revealed truncated mRNAs, including a frameshift. Alteration and inactivation of the FEZ1 gene may play a role in various human tumors. Ishii et al. (2001) showed that introduction of FEZ1/LZTS1 into FEZ1/LZTS1-negative cancer cells resulted in suppression

of tumorigenicity and reduced cell growth with accumulation of cells at late S-G2/M stage of the cell cycle. Their data showed that FEZ1/LZTS1 inhibits cancer cell growth through regulation of mitosis, and that its alterations result in abnormal cell growth. Ishii et al. (1999) analyzed the nucleotide sequence of the FEZ1 gene open reading frame in 194 cancers, including 72 primary esophageal cancers. They found a point mutation in 2 primary esophageal cancers and in a prostate cancer cell line.

[6782] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6783] Ishii, H.; Baffa, R.; Numata, S.-I.; Murakumo, Y.; Rattan, S.; Inoue, H.; Mori, M.; Fidanza, V.; Alder, H.; Croce, C. M. : The FEZ1 gene at chromosome 8p22 encodes a leucine-zipper protein, and its expression is altered in multiple human tumors. Proc. Nat. Acad. Sci. 96: 3928-3933, 1999. ; and

[6784] Ishii, H.; Vecchione, A.; Murakumo, Y.; Baldassarre, G.; Numata, S.; Trapasso, F.; Alder, H.; Baffa, R.; Croce, C. M. : FEZ1/LZTS1 gene at 8p22 suppresses cancer cell growth and regula.

[6785] Further studies establishing the function and utilities of

FEZ1 are found in John Hopkins OMIM database record ID 606551, and in cited publications numbered 4650 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 18 Receptor 1 (IL18R1, Accession NM_003855) is another VGAM37 host target gene. IL18R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL18R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL18R1 BINDING SITE, designated SEQ ID:9951, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6786] Another function of VGAM37 is therefore inhibition of Interleukin 18 Receptor 1 (IL18R1, Accession NM_003855), a gene which is required for dorsal-ventral embryonic polarity and promotes heterophilic cellular adhesion. Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL18R1. The function of IL18R1 has been established by previous studies. Using a YAC template known to contain IL1R1 (OMIM Ref. No. 147810), Parnet et

al. (1996) cloned by PCR with degenerate primers what was thought to be a member of the interleukin-1 receptor family, which they called IL1 receptor-related protein (OMIM Ref. No. IL1RRP). The gene encodes a 541-amino acid protein. Although the sequence was similar to that of IL1Rs, the extracellular portion failed to bind IL1A (OMIM Ref. No. 147760), IL1B (OMIM Ref. No. 147720), or IL1RN (OMIM Ref. No. 147679). When the cytoplasmic domain was fused to mouse IL1 extracellular and transmembrane portions, it activated NF-kappa-B (OMIM Ref. No. 164011) in response to IL1. Northern blot analysis revealed that IL1RRP is expressed in lung, leukocytes, spleen, liver, thymus, prostate, small intestine, colon, placenta, and heart, and is absent from brain, skeletal muscle, pancreas, and kidney. Torigoe et al. (1997) purified human IL18R, symbolized IL18R1, by selecting a Hodgkin disease cell line, L428, that was the best binder in IL18 (OMIM Ref. No. 600953) binding assays. The binding of radiolabeled IL18 was inhibited by IL18 but not by IL1B, with which it has 15% amino acid homology but no functional resemblance. The authors raised a monoclonal antibody against L428 cells and used it to purify IL18R from solubilized cells after wheat germ lectin chromatography. They found that

the internal amino acid sequence matched that of IL1RRP. When expressed in COS-1 cells, the cDNA of IL1RRP conferred IL18 binding properties and the ability to activate NF-kappa-B in response to IL18 but not IL1B.

[6787] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6788] Dale, M.; Nicklin, M. J. : Interleukin-1 receptor cluster: gene organization of IL1R2, IL1R1, IL1RL2 (IL-1Rrp2), IL1RL1 (T1/ST2), and IL18R1 (IL-1Rrp) on human chromosome 2q. Genomics 57: 177-179, 1999. ; and

[6789] Parnet, P.; Garka, K. E.; Bonnert, T. P.; Dower, S. K.; Sims, J. E. : IL-1Rrp is a novel receptor-like molecule similar to the type I interleukin-1 receptor and its homologues T1/ST2 an.

[6790] Further studies establishing the function and utilities of IL18R1 are found in John Hopkins OMIM database record ID 604494, and in cited publications numbered 304 and 5305-5306 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_133631) is another VGAM37 host target gene. ROBO1 BINDING SITE1 and

ROBO1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ROBO1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO1 BINDING SITE1 and ROBO1 BINDING SITE2, designated SEQ ID:28589 and SEQ ID:8852 respectively, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6791] Another function of VGAM37 is therefore inhibition of Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_133631), a gene which is an axon guidance receptor. Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO1. The function of ROBO1 has been established by previous studies. Using in situ hybridization analysis, Bagri et al. (2002) detected expression of Robo1 and Robo2 in the developing cortex and thalamus of mouse embryos. They detected a complementary pattern of expression of Robo and Slit genes (see OMIM Ref. No. Slit1; 603742) in the developing mouse forebrain and concluded that these molecules may play a role in the guidance of corticofugal

and thalamocortical projections Zallen et al. (1998) cloned a *C. elegans* gene, termed *sax3*, that is homologous to *ROBO1*. Mutations in *sax3* lead to repeated midline crossing by ventral cord axons that normally do not cross the midline after they join the ventral cord, a phenotype similar to that of *Drosophila robo* mutants. *Sax3* is also required for the guidance of some axons to the ventral cord, implicating this gene in 2 different types of guidance events. A *sax3*/GFP fusion gene is expressed in developing neurons during axon outgrowth, and *sax-3* function is required at the time of axon guidance. Zallen et al. (1998) concluded that in *C. elegans* this gene mediates cell interactions during guidance decisions.

[6792] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6793] Bagri, A.; Marin, O.; Plump, A. S.; Mak, J.; Pleasure, S. J.; Rubenstein, J. L. R.; Tessier-Lavigne, M. : Slit proteins prevent midline crossing and determine the dorsoventral position of major axonal pathways in the mammalian forebrain. *Neuron* 33: 233–248, 2002. ; and

[6794] Zallen, J. A.; Yi, B. A.; Bargmann, C. I. : The conserved immunoglobulin superfamily member *SAX-3*/Robo directs

multiple aspects of axon guidance in *C. elegans*. *Cell* 92: 217–227, 1998.

[6795] Further studies establishing the function and utilities of ROBO1 are found in John Hopkins OMIM database record ID 602430, and in cited publications numbered 8916–891 and 9113–8920 listed in the bibliography section herein–below, which are also hereby incorporated by reference. KIAA0923 (Accession NM_014021) is another VGAM37 host target gene. KIAA0923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0923 BINDING SITE, designated SEQ ID:15246, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6796] Another function of VGAM37 is therefore inhibition of KIAA0923 (Accession NM_014021). Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0923. KIAA1432 (Accession XM_039698) is another VGAM37 host target gene. KIAA1432 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1432 BINDING SITE, designated SEQ ID:33155, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6797] Another function of VGAM37 is therefore inhibition of KIAA1432 (Accession XM_039698). Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. LOC152559 (Accession XM_087487) is another VGAM37 host target gene. LOC152559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152559 BINDING SITE, designated SEQ ID:39285, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6798] Another function of VGAM37 is therefore inhibition of

LOC152559 (Accession XM_087487). Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152559. LOC197131 (Accession XM_113823) is another VGAM37 host target gene. LOC197131 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197131, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197131 BINDING SITE, designated SEQ ID:42445, to the nucleotide sequence of VGAM37 RNA, herein designated VGAM RNA, also designated SEQ ID:2748.

[6799] Another function of VGAM37 is therefore inhibition of LOC197131 (Accession XM_113823). Accordingly, utilities of VGAM37 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197131. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 38 (VGAM38) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[6800] VGAM38 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM38 was detected is described hereinabove with reference to Figs. 1–8.

[6801] VGAM38 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6802] VGAM38 gene encodes a VGAM38 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM38 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM38 precursor RNA is designated SEQ ID:24, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:24 is located at position 79915 relative to the genome of Invertebrate Iridescent Virus 6.

[6803] VGAM38 precursor RNA folds onto itself, forming VGAM38 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin

structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6804] An enzyme complex designated DICER COMPLEX, `dices` the VGAM38 folded precursor RNA into VGAM38 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM38 RNA is designated SEQ ID:2749, and is provided hereinbelow with reference to the sequence listing part.

[6805] VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM38 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3`

untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6806] VGAM38 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM38 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM38 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6807] The complementary binding of VGAM38 RNA, herein designated VGAM RNA, to host target binding sites on VGAM38 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM38 host target RNA into VGAM38 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6808] It is appreciated that VGAM38 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM38 host target genes. The mRNA of each one of this plurality of VGAM38 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM38 RNA, herein designated VGAM RNA, and which when bound by VGAM38 RNA causes inhibition of translation of respective one or more VGAM38 host target proteins.

[6809] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM38 gene, herein designated VGAM GENE, on one or more VGAM38 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6810] It is yet further appreciated that a function of VGAM38 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM38 correlate with, and may be deduced from, the identity of the host target genes which VGAM38 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6811] Nucleotide sequences of the VGAM38 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM38 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM38 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM38 are further described hereinbelow with reference to Table 1.

[6812] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM38 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM38 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6813] As mentioned hereinabove with reference to Fig. 1, a function of VGAM38 gene, herein designated VGAM is inhibition of expression of VGAM38 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM38 correlate with, and may be deduced from, the identity of the target genes which VGAM38 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6814] CLIPR-59 (Accession NM_015526) is a VGAM38 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59 BINDING SITE, designated SEQ ID:17791, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6815] A function of VGAM38 is therefore inhibition of CLIPR-59 (Accession NM_015526). Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. DKFZp547I014 (Accession NM_020217) is another VGAM38 host target gene. DKFZp547I014 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I014 BINDING SITE, designated SEQ ID:21468, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6816] Another function of VGAM38 is therefore inhibition of DKFZp547I014 (Accession NM_020217). Accordingly, utilities

of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DK-FZp547I014. FLJ11184 (Accession NM_018352) is another VGAM38 host target gene. FLJ11184 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11184, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11184 BINDING SITE, designated SEQ ID:20366, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6817] Another function of VGAM38 is therefore inhibition of FLJ11184 (Accession NM_018352). Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11184. KIAA0426 (Accession NM_014724) is another VGAM38 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE,

designated SEQ ID:16307, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6818] Another function of VGAM38 is therefore inhibition of KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA1354 (Accession XM_027604) is another VGAM38 host target gene. KIAA1354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1354 BINDING SITE, designated SEQ ID:30541, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6819] Another function of VGAM38 is therefore inhibition of KIAA1354 (Accession XM_027604). Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1354. LOC257058 (Accession XM_173738) is another VGAM38 host target gene. LOC257058 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257058 BINDING SITE, designated SEQ ID:46560, to the nucleotide sequence of VGAM38 RNA, herein designated VGAM RNA, also designated SEQ ID:2749.

[6820] Another function of VGAM38 is therefore inhibition of LOC257058 (Accession XM_173738). Accordingly, utilities of VGAM38 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257058. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 39 (VGAM39) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6821] VGAM39 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM39 was detected is described hereinabove with reference to Figs. 1-8.

[6822] VGAM39 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6823] VGAM39 gene encodes a VGAM39 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM39 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM39 precursor RNA is designated SEQ ID:25, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:25 is located at position 163620 relative to the genome of Invertebrate Iridescent Virus 6.

[6824] VGAM39 precursor RNA folds onto itself, forming VGAM39 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide

sequence of the second half thereof.

[6825] An enzyme complex designated DICER COMPLEX, `dices` the VGAM39 folded precursor RNA into VGAM39 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM39 RNA is designated SEQ ID:2750, and is provided hereinbelow with reference to the sequence listing part.

[6826] VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM39 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6827] VGAM39 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM39 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM39 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM39 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6828] The complementary binding of VGAM39 RNA, herein designated VGAM RNA, to host target binding sites on VGAM39 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM39 host tar-

get RNA into VGAM39 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6829] It is appreciated that VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM39 host target genes. The mRNA of each one of this plurality of VGAM39 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM39 RNA, herein designated VGAM RNA, and which when bound by VGAM39 RNA causes inhibition of translation of respective one or more VGAM39 host target proteins.

[6830] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM39 gene, herein designated VGAM GENE, on one or more VGAM39 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and

Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6831] It is yet further appreciated that a function of VGAM39 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM39 correlate with, and may be deduced from, the identity of the host target genes which VGAM39 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6832] Nucleotide sequences of the VGAM39 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM39 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM39 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM39 are further described hereinbelow with reference to Table 1.

[6833] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM39 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM39 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6834] As mentioned hereinabove with reference to Fig. 1, a function of VGAM39 gene, herein designated VGAM is inhibition of expression of VGAM39 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM39 correlate with, and may be deduced from, the identity of the target genes which VGAM39 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6835] Fibromodulin (FMOD, Accession NM_002023) is a VGAM39 host target gene. FMOD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FMOD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FMOD BINDING SITE, designated SEQ ID:7769, to the nucleotide sequence of

VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6836] A function of VGAM39 is therefore inhibition of Fibromodulin (FMOD, Accession NM_002023), a gene which affects the rate of fibrils formation. Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FMOD. The function of FMOD has been established by previous studies. Fibromodulin is a member of a family of small interstitial proteoglycans that also includes decorin (DCN; 125255), biglycan (BGN; 301870), and lumican (LDC; 600616). The core proteins of these proteoglycans are structurally related, consisting of a central region composed of leucine-rich repeats flanked by disulfide-bonded terminal domains, with that for fibromodulin possessing up to 4 keratan sulfate chains within its leucine-rich domain. Fibromodulin exhibits a wide tissue distribution, with the highest abundance observed in articular cartilage, tendon, and ligament. It has been suggested that fibromodulin participates in the assembly of the extracellular matrix by virtue of its ability to interact with type I and type II collagen fibrils and to inhibit fibrillogenesis in vitro. Sztrolovics et al. (1994) cloned the 3-prime untranslated

region of the fibromodulin cDNA. By fluorescence in situ hybridization, Sztrolovics et al. (1994) mapped the FMOD gene to 1q32. Secondary signals were detected at 9q34.1; however, PCR analysis of somatic cell hybrids confirmed the localization to chromosome 1. Animal model experiments lend further support to the function of FMOD. Lumican (OMIM Ref. No. 600616) and fibromodulin regulate the assembly of collagens into higher-order fibrils in connective tissues. Jepsen et al. (2002) found that mice in which the genes encoding both of these proteoglycans had been knocked out manifest several clinical features of Ehlers–Danlos syndrome (see OMIM Ref. No. 130000).

[6837] It is appreciated that the abovementioned animal model for FMOD is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6838] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6839] Jepsen, K. J.; Wu, F.; Peragallo, J. H.; Paul, J.; Roberts, L.; Ezura, Y.; Oldberg, A.; Birk, D. E.; Chakravarti, S. : A syndrome of joint laxity and impaired tendon integrity in lumican- and fibromodulin-deficient mice. J. Biol. Chem.

277: 35532–35540, 2002. ; and

[6840] Sztrolovics, R.; Chen, X.-N.; Grover, J.; Roughley, P. J.; Korenberg, J. R. : Localization of the human fibromodulin gene (FMOD) to chromosome 1q32 and completion of the cDNA sequence.

[6841] Further studies establishing the function and utilities of FMOD are found in John Hopkins OMIM database record ID 600245, and in cited publications numbered 7916–7917 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kallmann Syndrome 1 Sequence (KAL1, Accession NM_000216) is another VGAM39 host target gene. KAL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KAL1 BINDING SITE, designated SEQ ID:5715, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6842] Another function of VGAM39 is therefore inhibition of Kallmann Syndrome 1 Sequence (KAL1, Accession NM_000216). Accordingly, utilities of VGAM39 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with KAL1. Mab-21-like 1 (*C. elegans*) (MAB21L1, Accession NM_005584) is another VGAM39 host target gene. MAB21L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAB21L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAB21L1 BINDING SITE, designated SEQ ID:12111, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6843] Another function of VGAM39 is therefore inhibition of Mab-21-like 1 (*C. elegans*) (MAB21L1, Accession NM_005584), a gene which may control cerebellum and eye development; very strongly similar to murine Mm.10798. Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAB21L1. The function of MAB21L1 has been established by previous studies. Margolis et al. (1996) cloned the CAGR1 gene from a retinal cDNA library. The gene encodes a 359-amino acid protein that is homologous to the *C. elegans* cell fate-de-

termining protein mab-21 (56% identical and 81% conserved amino acids). Northern blot analysis revealed that CAGR1 is expressed in a number of tissues, with highest expression in the brain, particularly in the cerebellum. A CAG trinucleotide repeat occurs in the 5-prime untranslated region of CAGR1. This repeat is highly polymorphic, with alleles ranging from 6 to 31 repeats. Margolis et al. (1996) reported that an individual with an idiopathic movement disorder and affective disorder had an allele that contained 46 repeats. Potter (1997) analyzed 928 chromosomes from controls and patients with a variety of neurologic diseases. He found a normal CAG repeat size range of 9 to 29 repeats. One individual with developmental delay and mental retardation had 50 repeats; however, 3 other family members with alleles of similar size were apparently normal. Analysis of other family members showed meiotic stability for repeats of normal length and meiotic instability for alleles with 45 or more repeats. Margolis et al. (1999) reported a second pedigree with an expanded and unstably transmitted MAB21L1 CAG repeat. One individual from this pedigree was included in the report of Margolis et al. (1996). The expansion size ranged up to 51 repeats. The repeat length tended to increase in

subsequent generations, but the expanded allele was not associated with a phenotypic abnormality. The pedigree, however, was complex, with a number of individuals affected with neurologic and psychiatric disorders. Repeat length did not influence the level of MAB21L1 protein in lymphoblasts from 2 family members with an expanded MAB21L1 repeat. Margolis et al. (1999) hypothesized that the CAG repeat in MAB21L1 may behave as a premutation, and that longer expansions may be associated with a clinical phenotype.

[6844] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6845] Margolis, R. L.; Stine, O. C.; Ward, C. M.; Franz, M. L.; Rosenblatt, A.; Callahan, C.; Sherr, M.; Ross, C. A.; Potter, N. T. : Unstable expansion of the CAG trinucleotide repeat in MAB21L1: report of a second pedigree and effect on protein expression. J. Med. Genet. 36: 62–64, 1999. ; and

[6846] Margolis, R. L.; Stine, O. C.; McInnis, M. G.; Ranen, N. G.; Rubinsztein, D. C.; Leggo, J.; Brando, L. V. J.; Kidwai, A. S.; Loev, S. J.; Breschel, T. S.; Callahan, C.; Simpson, S. G.; and.

[6847] Further studies establishing the function and utilities of

MAB21L1 are found in John Hopkins OMIM database record ID 601280, and in cited publications numbered 1329–1328 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Matrix Metalloproteinase 14 (membrane-inserted) (MMP14, Accession NM_004995) is another VGAM39 host target gene. MMP14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MMP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP14 BINDING SITE, designated SEQ ID:11434, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6848] Another function of VGAM39 is therefore inhibition of Matrix Metalloproteinase 14 (membrane-inserted) (MMP14, Accession NM_004995). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP14. Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130833) is another VGAM39 host target gene. OPA1 BINDING SITE1 through OPA1 BINDING SITE5 are HOST

TARGET binding sites found in untranslated regions of mRNA encoded by OPA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA1 BINDING SITE1 through OPA1 BINDING SITE5, designated SEQ ID:28321, SEQ ID:28329, SEQ ID:28337, SEQ ID:28345 and SEQ ID:28353 respectively, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6849] Another function of VGAM39 is therefore inhibition of Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130833). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA1. Zinc Finger Protein 192 (ZNF192, Accession NM_006298) is another VGAM39 host target gene. ZNF192 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF192 BINDING SITE, designated SEQ ID:12986, to the nucleotide sequence of

VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6850] Another function of VGAM39 is therefore inhibition of Zinc Finger Protein 192 (ZNF192, Accession NM_006298). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF192. Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM_015049) is another VGAM39 host target gene. ALS2CR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALS2CR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2CR3 BINDING SITE, designated SEQ ID:17410, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6851] Another function of VGAM39 is therefore inhibition of Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM_015049). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with ALS2CR3. C3IP1 (Accession NM_021633) is another VGAM39 host target gene. C3IP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C3IP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C3IP1 BINDING SITE, designated SEQ ID:22273, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6852] Another function of VGAM39 is therefore inhibition of C3IP1 (Accession NM_021633). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C3IP1. DKFZp761J139 (Accession NM_032280) is another VGAM39 host target gene. DKFZp761J139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761J139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761J139 BINDING SITE, designated SEQ ID:26035, to the nucleotide sequence of VGAM39 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2750.

[6853] Another function of VGAM39 is therefore inhibition of DK-FZp761J139 (Accession NM_032280). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DK-FZp761J139. FLJ10468 (Accession NM_018101) is another VGAM39 host target gene. FLJ10468 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10468 BINDING SITE, designated SEQ ID:19873, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6854] Another function of VGAM39 is therefore inhibition of FLJ10468 (Accession NM_018101). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10468. FLJ10781 (Accession NM_018215) is another VGAM39 host target gene. FLJ10781 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10781, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10781 BINDING SITE, designated SEQ ID:20133, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6855] Another function of VGAM39 is therefore inhibition of FLJ10781 (Accession NM_018215). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10781. FLJ11175 (Accession NM_018349) is another VGAM39 host target gene. FLJ11175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11175 BINDING SITE, designated SEQ ID:20361, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6856] Another function of VGAM39 is therefore inhibition of FLJ11175 (Accession NM_018349). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ11175. FLJ20972 (Accession NM_025030) is another VGAM39 host target gene. FLJ20972 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20972 BINDING SITE, designated SEQ ID:24625, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6857] Another function of VGAM39 is therefore inhibition of FLJ20972 (Accession NM_025030). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20972. FLJ23233 (Accession NM_024691) is another VGAM39 host target gene. FLJ23233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23233 BINDING SITE, designated SEQ ID:23999, to the nucleotide sequence of

VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6858] Another function of VGAM39 is therefore inhibition of FLJ23233 (Accession NM_024691). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23233. HRIHFB2122 (Accession NM_007032) is another VGAM39 host target gene. HRIHFB2122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRIHFB2122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRIHFB2122 BINDING SITE, designated SEQ ID:13897, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6859] Another function of VGAM39 is therefore inhibition of HRIHFB2122 (Accession NM_007032). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRIHFB2122. KIAA0016 (Accession NM_014765) is another VGAM39 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16529, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6860] Another function of VGAM39 is therefore inhibition of KIAA0016 (Accession NM_014765). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. KIAA0459 (Accession XM_027862) is another VGAM39 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30572, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6861] Another function of VGAM39 is therefore inhibition of KIAA0459 (Accession XM_027862). Accordingly, utilities

of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0459. KIAA0712 (Accession NM_014715) is another VGAM39 host target gene. KIAA0712 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0712 BINDING SITE, designated SEQ ID:16263, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6862] Another function of VGAM39 is therefore inhibition of KIAA0712 (Accession NM_014715). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0712. KIAA0773 (Accession NM_014690) is another VGAM39 host target gene. KIAA0773 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0773 BINDING SITE, designated SEQ ID:16194, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6863] Another function of VGAM39 is therefore inhibition of KIAA0773 (Accession NM_014690). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0773. KIAA0930 (Accession XM_047214) is another VGAM39 host target gene. KIAA0930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0930 BINDING SITE, designated SEQ ID:34912, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6864] Another function of VGAM39 is therefore inhibition of KIAA0930 (Accession XM_047214). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0930. KIAA0976 (Accession NM_014917) is another VGAM39 host target gene. KIAA0976 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0976, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0976 BINDING SITE, designated SEQ ID:17164, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6865] Another function of VGAM39 is therefore inhibition of KIAA0976 (Accession NM_014917). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0976. KIAA1046 (Accession NM_014928) is another VGAM39 host target gene. KIAA1046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1046 BINDING SITE, designated SEQ ID:17219, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6866] Another function of VGAM39 is therefore inhibition of

KIAA1046 (Accession NM_014928). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1046. KIAA1143 (Accession XM_044014) is another VGAM39 host target gene. KIAA1143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1143 BINDING SITE, designated SEQ ID:34072, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6867] Another function of VGAM39 is therefore inhibition of KIAA1143 (Accession XM_044014). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1143. KIAA1580 (Accession XM_045271) is another VGAM39 host target gene. KIAA1580 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1580 BINDING SITE, designated SEQ ID:34410, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6868] Another function of VGAM39 is therefore inhibition of KIAA1580 (Accession XM_045271). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1580. KIAA1715 (Accession XM_042834) is another VGAM39 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33788, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6869] Another function of VGAM39 is therefore inhibition of KIAA1715 (Accession XM_042834). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. Phospholipid Scramblase 4 (PLSCR4, Accession

NM_020353) is another VGAM39 host target gene. PLSCR4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLSCR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR4 BINDING SITE, designated SEQ ID:21621, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6870] Another function of VGAM39 is therefore inhibition of Phospholipid Scramblase 4 (PLSCR4, Accession NM_020353). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR4. Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM_024430) is another VGAM39 host target gene. PSTPIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSTPIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSTPIP2 BINDING SITE, designated SEQ ID:23679, to the nucleotide sequence of VGAM39 RNA,

herein designated VGAM RNA, also designated SEQ ID:2750.

[6871] Another function of VGAM39 is therefore inhibition of Proline-serine-threonine Phosphatase Interacting Protein 2 (PSTPIP2, Accession NM_024430). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PST-PIP2. Retinoic Acid Induced 15 (RAI15, Accession XM_039548) is another VGAM39 host target gene. RAI15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI15 BINDING SITE, designated SEQ ID:33116, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6872] Another function of VGAM39 is therefore inhibition of Retinoic Acid Induced 15 (RAI15, Accession XM_039548). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI15. RNAH (Accession XM_030392) is another VGAM39 host target gene. RNAH BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAH BINDING SITE, designated SEQ ID:31037, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6873] Another function of VGAM39 is therefore inhibition of RNAH (Accession XM_030392). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNAH. SSH1 (Accession NM_018984) is another VGAM39 host target gene. SSH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH1 BINDING SITE, designated SEQ ID:21054, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6874] Another function of VGAM39 is therefore inhibition of

SSH1 (Accession NM_018984). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH1. TUBB5 (Accession NM_006087) is another VGAM39 host target gene. TUBB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUBB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUBB5 BINDING SITE, designated SEQ ID:12728, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6875] Another function of VGAM39 is therefore inhibition of TUBB5 (Accession NM_006087). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUBB5. LOC112687 (Accession XM_053145) is another VGAM39 host target gene. LOC112687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC112687 BINDING SITE, designated SEQ ID:36065, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6876] Another function of VGAM39 is therefore inhibition of LOC112687 (Accession XM_053145). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112687. LOC127602 (Accession XM_059166) is another VGAM39 host target gene. LOC127602 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC127602, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127602 BINDING SITE, designated SEQ ID:36903, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6877] Another function of VGAM39 is therefore inhibition of LOC127602 (Accession XM_059166). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127602. LOC143425 (Accession XM_113695) is an-

other VGAM39 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143425 BINDING SITE, designated SEQ ID:42350, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6878] Another function of VGAM39 is therefore inhibition of LOC143425 (Accession XM_113695). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC145725 (Accession XM_085211) is another VGAM39 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37946, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6879] Another function of VGAM39 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM39 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37955, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6880] Another function of VGAM39 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC151623 (Accession XM_098096) is another VGAM39 host target gene. LOC151623 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151623, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151623 BINDING SITE, designated SEQ ID:41378, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6881] Another function of VGAM39 is therefore inhibition of LOC151623 (Accession XM_098096). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151623. LOC196957 (Accession XM_113789) is another VGAM39 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42428, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6882] Another function of VGAM39 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC196957. LOC196961 (Accession XM_113790) is another VGAM39 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42437, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6883] Another function of VGAM39 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM39 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42455, to the nucleotide sequence of VGAM39 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2750.

[6884] Another function of VGAM39 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC197414 (Accession XM_113880) is another VGAM39 host target gene. LOC197414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197414 BINDING SITE, designated SEQ ID:42513, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6885] Another function of VGAM39 is therefore inhibition of LOC197414 (Accession XM_113880). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197414. LOC219406 (Accession XM_167976) is another VGAM39 host target gene. LOC219406 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219406, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219406 BINDING SITE, designated SEQ ID:44939, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6886] Another function of VGAM39 is therefore inhibition of LOC219406 (Accession XM_167976). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219406. LOC222486 (Accession XM_169432) is another VGAM39 host target gene. LOC222486 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222486 BINDING SITE, designated SEQ ID:45299, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6887] Another function of VGAM39 is therefore inhibition of LOC222486 (Accession XM_169432). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC222486. LOC253731 (Accession XM_173777) is another VGAM39 host target gene. LOC253731 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253731, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253731 BINDING SITE, designated SEQ ID:46562, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6888] Another function of VGAM39 is therefore inhibition of LOC253731 (Accession XM_173777). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253731. LOC255461 (Accession XM_173207) is another VGAM39 host target gene. LOC255461 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255461 BINDING SITE, designated SEQ ID:46464, to

the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6889] Another function of VGAM39 is therefore inhibition of LOC255461 (Accession XM_173207). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255461. LOC255516 (Accession XM_173212) is another VGAM39 host target gene. LOC255516 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255516 BINDING SITE, designated SEQ ID:46470, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6890] Another function of VGAM39 is therefore inhibition of LOC255516 (Accession XM_173212). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255516. LOC92095 (Accession XM_042811) is another VGAM39 host target gene. LOC92095 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC92095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92095 BINDING SITE, designated SEQ ID:33773, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6891] Another function of VGAM39 is therefore inhibition of LOC92095 (Accession XM_042811). Accordingly, utilities of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92095. LOC92096 (Accession XM_042812) is another VGAM39 host target gene. LOC92096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92096 BINDING SITE, designated SEQ ID:33776, to the nucleotide sequence of VGAM39 RNA, herein designated VGAM RNA, also designated SEQ ID:2750.

[6892] Another function of VGAM39 is therefore inhibition of LOC92096 (Accession XM_042812). Accordingly, utilities

of VGAM39 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92096. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 40 (VGAM40) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6893] VGAM40 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM40 was detected is described hereinabove with reference to Figs. 1–8.

[6894] VGAM40 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6895] VGAM40 gene encodes a VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM40 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM40 precursor RNA is designated SEQ ID:26, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:26 is located at position 36563 relative to the genome of Invertebrate Iridescent Virus 6.

[6896] VGAM40 precursor RNA folds onto itself, forming VGAM40 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6897] An enzyme complex designated DICER COMPLEX, `dices` the VGAM40 folded precursor RNA into VGAM40 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM40 RNA is designated SEQ ID:2751, and is

provided hereinbelow with reference to the sequence listing part.

[6898] VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM40 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6899] VGAM40 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM40 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM40 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6900] The complementary binding of VGAM40 RNA, herein designated VGAM RNA, to host target binding sites on VGAM40 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM40 host target RNA into VGAM40 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6901] It is appreciated that VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM40 host target genes. The mRNA of each one of this plurality of VGAM40 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM40 RNA, herein designated VGAM

RNA, and which when bound by VGAM40 RNA causes inhibition of translation of respective one or more VGAM40 host target proteins.

[6902] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM40 gene, herein designated VGAM GENE, on one or more VGAM40 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6903] It is yet further appreciated that a function of VGAM40 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM40 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM40 correlate with, and may be deduced from, the identity of the host target genes which VGAM40 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6904] Nucleotide sequences of the VGAM40 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM40 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM40 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM40 are further described hereinbelow with reference to Table 1.

[6905] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM40 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM40 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6906] As mentioned hereinabove with reference to Fig. 1, a function of VGAM40 gene, herein designated VGAM is inhibition of expression of VGAM40 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM40 correlate with, and may be deduced from, the identity of the target genes which VGAM40 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6907] Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692) is a VGAM40 host target gene. ALDH1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH1B1 BINDING SITE, designated SEQ ID:6348, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6908] A function of VGAM40 is therefore inhibition of Aldehyde Dehydrogenase 1 Family, Member B1 (ALDH1B1, Accession NM_000692). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH1B1. Mel Transforming Oncogene (derived from cell line NK14)– RAB8 Homolog (MEL, Accession NM_005370) is another

VGAM40 host target gene. MEL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEL BINDING SITE, designated SEQ ID:11842, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6909] Another function of VGAM40 is therefore inhibition of Mel Transforming Oncogene (derived from cell line NK14)-RAB8 Homolog (MEL, Accession NM_005370), a gene which may be involved in vesicular trafficking and neurotransmitter release. Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEL. The function of MEL has been established by previous studies. Members of the RAS superfamily are small GTP/GDP-binding proteins with an average size of 200 amino acids. The RAS-related proteins of the RAB/YPT family may play a role in the transport of proteins from the endoplasmic reticulum to the Golgi and the plasma membrane. See RAB5 (OMIM Ref. No. 179512). Using DNA transfection into NIH 3T3

cells, Padua et al. (1984) demonstrated that the human malignant melanoma cell line NK14 contains a novel transforming gene. Nimmo et al. (1991) isolated human MEL genomic clones and cDNAs, as well as a cDNA encoding the mouse MEL homolog. The predicted 206-amino acid human MEL protein shares 97%, 96%, and 51% identity with the dog RAB8, mouse MEL, and mouse YPT1 (RAB1; 179508) proteins, respectively. MEL contains the 4 GTP/GDP-binding sites that are present in all the RAS proteins. The putative effector-binding site of MEL is similar to that of the RAB/YPT proteins. However, MEL contains a C-terminal CAAX motif that is characteristic of many RAS superfamily members but which is not found in YPT1 and the majority of RAB proteins. Although MEL was isolated as a transforming gene from a melanoma cell line, no linkage between MEL and malignant melanoma (OMIM Ref. No. 155600) was demonstrable (Nimmo et al., 1989). As a result of studies of human-mouse and human-hamster somatic cell hybrids, Spurr et al. (1986) demonstrated that the MEL oncogene is located in the segment 19p13.2-q13.2. By linkage analysis using an NcoI RFLP, Nimmo et al. (1989, 1989) mapped the MEL gene to the region of LDLR (OMIM Ref. No. 606945), i.e.,

19p13.2–cen. Nimmo et al. (1991) noted that the human RAB3A (OMIM Ref. No. 179490) gene has been localized to 19p13.2. Bahler et al. (1997) performed cosmid contig mapping indicating that the MEL locus was 800 kb distal to MY09B (OMIM Ref. No. 602129) on chromosome 19p13.1.

[6910] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6911] Padua, R. A.; Barrass, N.; Currie, G. A. : A novel transforming gene in a human malignant melanoma cell line. *Nature* 311: 671–673, 1984. ; and

[6912] Nimmo, E. R.; Sanders, P. G.; Padua, R. A.; Hughes, D.; Williamson, R.; Johnson, K. J. : The MEL gene: a new member of the RAB/YPT class of RAS–related genes. *Oncogene* 6: 1347–1351, 1991.

[6913] Further studies establishing the function and utilities of MEL are found in John Hopkins OMIM database record ID 165040, and in cited publications numbered 402 and 11533–11537 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitination Factor E4B (UFD2 homolog, yeast) (UBE4B, Accession NM_006048) is another VGAM40 host

target gene. UBE4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4B BINDING SITE, designated SEQ ID:12681, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6914] Another function of VGAM40 is therefore inhibition of Ubiquitination Factor E4B (UFD2 homolog, yeast) (UBE4B, Accession NM_006048). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE4B. LOC146517 (Accession XM_085491) is another VGAM40 host target gene. LOC146517 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146517, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146517 BINDING SITE, designated SEQ ID:38181, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2751.

[6915] Another function of VGAM40 is therefore inhibition of LOC146517 (Accession XM_085491). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146517. LOC158230 (Accession XM_088517) is another VGAM40 host target gene. LOC158230 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158230, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158230 BINDING SITE, designated SEQ ID:39765, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6916] Another function of VGAM40 is therefore inhibition of LOC158230 (Accession XM_088517). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158230. LOC204970 (Accession XM_114795) is another VGAM40 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204970, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43067, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6917] Another function of VGAM40 is therefore inhibition of LOC204970 (Accession XM_114795). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC254065 (Accession XM_173239) is another VGAM40 host target gene. LOC254065 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254065 BINDING SITE, designated SEQ ID:46521, to the nucleotide sequence of VGAM40 RNA, herein designated VGAM RNA, also designated SEQ ID:2751.

[6918] Another function of VGAM40 is therefore inhibition of LOC254065 (Accession XM_173239). Accordingly, utilities of VGAM40 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC254065. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 41 (VGAM41) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6919] VGAM41 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM41 was detected is described hereinabove with reference to Figs. 1–8.

[6920] VGAM41 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6921] VGAM41 gene encodes a VGAM41 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM41 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM41 precursor RNA is designated SEQ

ID:27, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:27 is located at position 108544 relative to the genome of Invertebrate Iridescent Virus 6.

[6922] VGAM41 precursor RNA folds onto itself, forming VGAM41 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6923] An enzyme complex designated DICER COMPLEX, `dices` the VGAM41 folded precursor RNA into VGAM41 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM41 RNA is designated SEQ ID:2752, and is provided hereinbelow with reference to the sequence list-

ing part.

[6924] VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM41 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6925] VGAM41 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM41 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM41 RNA, herein designated VGAM RNA, may have a different num-

ber of host target binding sites in untranslated regions of a VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6926] The complementary binding of VGAM41 RNA, herein designated VGAM RNA, to host target binding sites on VGAM41 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM41 host target RNA into VGAM41 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6927] It is appreciated that VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM41 host target genes. The mRNA of each one of this plurality of VGAM41 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM41 RNA, herein designated VGAM RNA, and which when bound by VGAM41 RNA causes in–

hibition of translation of respective one or more VGAM41 host target proteins.

[6928] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM41 gene, herein designated VGAM GENE, on one or more VGAM41 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6929] It is yet further appreciated that a function of VGAM41 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM41 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM41 correlate with, and may be deduced from, the identity of the host target genes which VGAM41 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6930] Nucleotide sequences of the VGAM41 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM41 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM41 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM41 are further described hereinbelow with reference to Table 1.

[6931] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM41 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM41 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6932] As mentioned hereinabove with reference to Fig. 1, a function of VGAM41 gene, herein designated VGAM is inhibition of expression of VGAM41 target genes. It is appreciated that specific functions, and accordingly utilities,

of VGAM41 correlate with, and may be deduced from, the identity of the target genes which VGAM41 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6933] Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538) is a VGAM41 host target gene. ERMAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERMAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERMAP BINDING SITE, designated SEQ ID:20607, to the nucleotide sequence of VGAM41 RNA, herein designated VGAM RNA, also designated SEQ ID:2752.

[6934] A function of VGAM41 is therefore inhibition of Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538). Accordingly, utilities of VGAM41 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERMAP. Rab11-FIP3 (Accession NM_014700) is another VGAM41 host target gene. Rab11-FIP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

Rab11-FIP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP3 BINDING SITE, designated SEQ ID:16226, to the nucleotide sequence of VGAM41 RNA, herein designated VGAM RNA, also designated SEQ ID:2752.

[6935] Another function of VGAM41 is therefore inhibition of Rab11-FIP3 (Accession NM_014700). Accordingly, utilities of VGAM41 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11-FIP3. LOC85028 (Accession NM_053040) is another VGAM41 host target gene. LOC85028 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC85028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85028 BINDING SITE, designated SEQ ID:27584, to the nucleotide sequence of VGAM41 RNA, herein designated VGAM RNA, also designated SEQ ID:2752.

[6936] Another function of VGAM41 is therefore inhibition of LOC85028 (Accession NM_053040). Accordingly, utilities

of VGAM41 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85028. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 42 (VGAM42) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6937] VGAM42 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM42 was detected is described hereinabove with reference to Figs. 1–8.

[6938] VGAM42 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6939] VGAM42 gene encodes a VGAM42 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM42 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM42 precursor RNA is designated SEQ ID:28, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:28 is located at position 82865 relative to the genome of Invertebrate Iridescent Virus 6.

[6940] VGAM42 precursor RNA folds onto itself, forming VGAM42 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6941] An enzyme complex designated DICER COMPLEX, `dices` the VGAM42 folded precursor RNA into VGAM42 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM42 RNA is designated SEQ ID:2753, and is

provided hereinbelow with reference to the sequence listing part.

[6942] VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM42 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6943] VGAM42 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM42 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM42 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[6944] The complementary binding of VGAM42 RNA, herein designated VGAM RNA, to host target binding sites on VGAM42 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM42 host target RNA into VGAM42 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6945] It is appreciated that VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM42 host target genes. The mRNA of each one of this plurality of VGAM42 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM42 RNA, herein designated VGAM

RNA, and which when bound by VGAM42 RNA causes inhibition of translation of respective one or more VGAM42 host target proteins.

[6946] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM42 gene, herein designated VGAM GENE, on one or more VGAM42 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6947] It is yet further appreciated that a function of VGAM42 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM42 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM42 correlate with, and may be deduced from, the identity of the host target genes which VGAM42 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[6948] Nucleotide sequences of the VGAM42 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM42 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM42 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM42 are further described hereinbelow with reference to Table 1.

[6949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM42 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM42 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6950] As mentioned hereinabove with reference to Fig. 1, a function of VGAM42 gene, herein designated VGAM is inhibition of expression of VGAM42 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM42 correlate with, and may be deduced from, the identity of the target genes which VGAM42 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[6951] Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM_033096) is a VGAM42 host target gene. CLTCL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLTCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLTCL1 BINDING SITE, designated SEQ ID:31835, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6952] A function of VGAM42 is therefore inhibition of Clathrin, Heavy Polypeptide-like 1 (CLTCL1, Accession XM_033096), a gene which is involved in vesicle budding. Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLTCL1. The function of CLTCL1 has been established by previous studies. Clathrin is the main structural component of the lattice covering the cytoplas-

mic face of the coated pits and coated vesicles in which specific macromolecules are entrapped in the process of receptor-mediated endocytosis. Clathrin is a large, soluble protein composed of heavy chains (molecular size, about 192 kD) and light chains (molecular size, about 32–38 kD). Two major classes of clathrin light chains, referred to as LCA and LCB, have been identified. (The gene is also symbolized CLTA.) The structure of these light chains was studied by Kirchhausen et al. (1987). The clathrin unit that assembles into coats had 3 extended legs, 500 angstroms in length, splayed out in a pinwheel-like structure (triskelion). Each of the legs is built from a single heavy chain, with a light chain bound to each proximal segment. At least 4 distinct forms of clathrin light chains are found in mammalian cells. This molecular variability derives from tissue-specific patterns of expression of LCA and LCB genes (Jackson et al., 1987). Brodsky et al. (1987) identified that part of the light-chain sequence that mediates heavy-chain binding and is the region of strongest homology with intermediate filament proteins. Sequence analysis shows an overall homology of 60% between LCA and LCB and the presence of brain-specific insertion sequences. LCA and LCB (OMIM Ref. No. 118970)

are coded by distinct genes. Jackson and Parham (1988) compared cDNAs encoding the brain and nonbrain forms of human LCA and LCB with their homologs in cow and rat. The significant differences that distinguish LCA from LCB and the brain from the nonbrain forms show remarkable preservation in all 3 species. Each clathrin triskelion consists of 3 heavy chains and 3 light chains. In the brain, tissue-specific mRNA splicing yields larger forms of LCA and LCB, containing additional insertion sequences of 30 and 18 amino acids, respectively. By Southern blot analysis on genomic DNA extracted from a panel of mouse-human somatic cell hybrids and by isotopic in situ hybridization, Ponnambalam et al. (1994) assigned the CLTA gene to human 12q23-q24

[6953] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6954] Sirotkin, H.; Morrow, B.; DasGupta, R.; Goldberg, R.; Patanjali, S. R.; Shi, G.; Cannizzaro, L.; Shprintzen, R.; Weissman, S. M.; Kucherlapati, R. : Isolation of a new clathrin heavy chain gene with muscle-specific expression from the region commonly deleted in velo-cardio-facial syndrome. Hum. Molec. Genet. 5: 617-624, 1996. ; and

[6955] Long, K. R.; Trofatter, J. A.; Ramesh, V.; McCormick, M. K.; Buckler, A. J. : Cloning and characterization of a novel human clathrin heavy chain gene (CLTCL). Genomics 35: 466–472, 1996.

[6956] Further studies establishing the function and utilities of CLTCL1 are found in John Hopkins OMIM database record ID 601273, and in cited publications numbered 9859–986 and 4066 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_130436) is another VGAM42 host target gene. DYRK1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28188, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6957] Another function of VGAM42 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_130436), a gene which

regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A has been established by previous studies. Shindoh et al. (1996) performed exon trapping to find exons within YAC clones spanning the 2-Mb 'Down syndrome critical region' (OMIM Ref. No. 190685) of human chromosome 21. Of more than 160 exons isolated, they found 6 that had significant identity at the amino acid level to the *Drosophila* 'minibrain' gene. Using 1 of these exons as a probe, they cloned the full-length human cDNA from a human fetal brain cDNA library. Sequence analysis of this cDNA revealed an open reading frame encoding a polypeptide of 754 amino acids. Shindoh et al. (1996) stated that this gene, termed MNB by them, represents the human homolog of the *Drosophila* *mnb* gene and of the rat *Dyrk* gene. The rat *Dyrk* gene differs from it by only 4 amino acids. Northern blot analysis of MNB revealed 2 transcripts of 6.0 and 7.5 kb. The 6.0-kb transcript was found to be present in all tissues examined, with highest levels of expression in skeletal muscle, testis, fetal lung, and fetal kidney. The 7.5-kb transcript was found to be

expressed at a relatively lower level and was found only in adult heart, placenta, spleen, and testis. Shindoh et al. (1996) concluded that the human MNB protein may play a significant role in a signaling pathway regulating cell proliferation and may be involved in normal brain development and in the pathogenesis of Down syndrome. Animal model experiments lend further support to the function of DYRK1A. Using Down syndrome as a model for complex trait analysis, Smith et al. (1997) sought to identify loci from 21q22.2 which, when present in an extra dose, contribute to learning abnormalities. They generated low-copy number transgenic mice, containing 4 different YACs that together cover approximately 2 Mb of contiguous DNA from 21q22.2. They subjected independent mouse lines derived from each of these YAC transgenes to a series of behavioral and learning assays. Two of the 4 YACs caused defects in learning and memory in the transgenic animals, while the other 2 YACs had no effect. The most severe defects were caused by a 570-kb YAC; the interval responsible for these defects was narrowed to a 180-kb critical region as a consequence of YAC fragmentation. This region was found to contain the human homolog of the *Drosophila* 'minibrain' gene, and strongly implicated it

in learning defects associated with Down syndrome.

[6958] It is appreciated that the abovementioned animal model for DYRK1A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[6959] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6960] Shindoh, N.; Kudoh, J.; Maeda, H.; Yamaki, A.; Minoshima, S.; Shimizu, Y.; Shimizu, N. : Cloning of a human homolog of the Drosophila minibrain/rat Dyrk gene from 'the Down syndrome critical region' of chromosome 21. Biochem. Biophys. Res. Commun. 225: 92–99, 1996. ; and

[6961] Smith, D. J.; Stevens, M. E.; Sudanagunta, S. P.; Bronson, R. T.; Makhinson, M.; Watabe, A. M.; O'Dell, T. J.; Fung, J.; Weier, H.–U. G.; Cheng, J.–F.; Rubin, E. M. : Functional screeni.

[6962] Further studies establishing the function and utilities of DYRK1A are found in John Hopkins OMIM database record ID 600855, and in cited publications numbered 774, 10065–10067, 1007 and 10071 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lipin 2 (LPIN2, Accession NM_014646) is an–

other VGAM42 host target gene. LPIN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN2 BINDING SITE, designated SEQ ID:16063, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6963] Another function of VGAM42 is therefore inhibition of Lipin 2 (LPIN2, Accession NM_014646). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPIN2. Osteomodulin (OMD, Accession NM_005014) is another VGAM42 host target gene. OMD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OMD BINDING SITE, designated SEQ ID:11455, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6964] Another function of VGAM42 is therefore inhibition of Osteomodulin (OMD, Accession NM_005014). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OMD. Zinc Finger Protein 304 (ZNF304, Accession NM_020657) is another VGAM42 host target gene. ZNF304 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF304, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF304 BINDING SITE, designated SEQ ID:21828, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6965] Another function of VGAM42 is therefore inhibition of Zinc Finger Protein 304 (ZNF304, Accession NM_020657). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF304. LOC150622 (Accession XM_086960) is another VGAM42 host target gene. LOC150622 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

LOC150622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150622 BINDING SITE, designated SEQ ID:38998, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6966] Another function of VGAM42 is therefore inhibition of LOC150622 (Accession XM_086960). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150622. LOC152925 (Accession XM_087559) is another VGAM42 host target gene. LOC152925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152925 BINDING SITE, designated SEQ ID:39330, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6967] Another function of VGAM42 is therefore inhibition of LOC152925 (Accession XM_087559). Accordingly, utilities

of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152925. LOC205355 (Accession XM_119694) is another VGAM42 host target gene. LOC205355 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC205355, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205355 BINDING SITE, designated SEQ ID:43596, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6968] Another function of VGAM42 is therefore inhibition of LOC205355 (Accession XM_119694). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205355. LOC220766 (Accession XM_165471) is another VGAM42 host target gene. LOC220766 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220766, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220766 BINDING SITE, designated SEQ ID:43648, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6969] Another function of VGAM42 is therefore inhibition of LOC220766 (Accession XM_165471). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220766. LOC92270 (Accession XM_043989) is another VGAM42 host target gene. LOC92270 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92270, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92270 BINDING SITE, designated SEQ ID:34062, to the nucleotide sequence of VGAM42 RNA, herein designated VGAM RNA, also designated SEQ ID:2753.

[6970] Another function of VGAM42 is therefore inhibition of LOC92270 (Accession XM_043989). Accordingly, utilities of VGAM42 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92270. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 43 (VGAM43) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6971] VGAM43 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM43 was detected is described hereinabove with reference to Figs. 1–8.

[6972] VGAM43 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6973] VGAM43 gene encodes a VGAM43 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM43 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM43 precursor RNA is designated SEQ ID:29, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:29 is located at position 189040 relative to the genome of In-

vertebrate Iridescent Virus 6.

[6974] VGAM43 precursor RNA folds onto itself, forming VGAM43 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6975] An enzyme complex designated DICER COMPLEX, `dices` the VGAM43 folded precursor RNA into VGAM43 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM43 RNA is designated SEQ ID:2754, and is provided hereinbelow with reference to the sequence listing part.

[6976] VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM43 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[6977] VGAM43 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM43 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM43 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig.

1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[6978] The complementary binding of VGAM43 RNA, herein designated VGAM RNA, to host target binding sites on VGAM43 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM43 host target RNA into VGAM43 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[6979] It is appreciated that VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM43 host target genes. The mRNA of each one of this plurality of VGAM43 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM43 RNA, herein designated VGAM RNA, and which when bound by VGAM43 RNA causes inhibition of translation of respective one or more VGAM43 host target proteins.

[6980] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM43 gene, herein designated VGAM GENE, on one or more VGAM43 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[6981] It is yet further appreciated that a function of VGAM43 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM43 correlate with, and may be deduced from, the identity of the host target genes which VGAM43 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[6982] Nucleotide sequences of the VGAM43 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM43 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM43 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM43 are further described hereinbelow with reference to Table 1.

[6983] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM43 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM43 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[6984] As mentioned hereinabove with reference to Fig. 1, a function of VGAM43 gene, herein designated VGAM is inhibition of expression of VGAM43 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM43 correlate with, and may be deduced from, the identity of the target genes which VGAM43 binds and inhibits, and the function of these target genes, as elabo-

rated hereinbelow.

[6985] Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410) is a VGAM43 host target gene. MGAT5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGAT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT5 BINDING SITE, designated SEQ ID:8237, to the nucleotide sequence of VGAM43 RNA, herein designated VGAM RNA, also designated SEQ ID:2754.

[6986] A function of VGAM43 is therefore inhibition of Mannosyl (alpha-1,6-)-glycoprotein Beta-1,6-N-acetyl-glucosaminyltransferase (MGAT5, Accession NM_002410). Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT5. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Zeta Polypeptide (YWHAZ, Accession NM_003406) is another VGAM43 host target gene. YWHAZ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAZ, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YWHAZ BINDING SITE, designated SEQ ID:9443, to the nucleotide sequence of VGAM43 RNA, herein designated VGAM RNA, also designated SEQ ID:2754.

[6987] Another function of VGAM43 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Zeta Polypeptide (YWHAZ, Accession NM_003406), a gene which mediates signal transduction by binding to phosphorylated serine residues on a variety of signaling molecules. Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAZ. The function of YWHAZ has been established by previous studies. The binding of insulin (OMIM Ref. No. 176730) to its receptor induces the phosphorylation of the cytosolic substrates IRS1 (OMIM Ref. No. 147545) and IRS2 (OMIM Ref. No. 600797), which associate with several Src homology-2 (SH2) domain-containing proteins. To identify unique IRS1-binding proteins, Ogihara et al. (1997) screened a human heart cDNA expression library with recombinant IRS1. They obtained 2 isoforms of the 14-3-3 protein

family, 14-3-3-zeta and -epsilon (YWHAE; 605066).

14-3-3 protein has been shown to associate with IRS1 in L6 myotubes, HepG2 hepatoma cells, Chinese hamster ovary cells, and bovine brain tissue. The amount of 14-3-3 protein associated with IRS1 was not affected by insulin stimulation but was increased significantly by treatment with okadaic acid, a potent serine/threonine phosphatase inhibitor. The authors identified a putative 14-3-3 protein-binding site within the phosphotyrosine-binding (PTB) domain of IRS1. Ogiwara et al. (1997) suggested that the association with 14-3-3 protein may play a role in the regulation of insulin sensitivity by interrupting the association between the insulin receptor and IRS1. Using in vitro pull-down assays, Powell et al. (2002) showed that recombinant 14-3-3-zeta interacted directly with both recombinant and endogenous protein kinase B (PKB, or AKT1; 164730) within embryonic kidney cell lysates. They found that recombinant PKB phosphorylated 14-3-3-zeta in an in vitro kinase assay, and transfection of active PKB into embryonic kidney cells resulted in phosphorylation of 14-3-3-zeta. By mutation analysis, Powell et al. (2002) determined that the phosphate acceptor was serine-58. They also showed that phosphorylation did not result in

14-3-3-zeta dimerization.

[6988] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[6989] Ogihara, T.; Isobe, T.; Ichimura, T.; Taoka, M.; Funaki, M.; Sakoda, H.; Onishi, Y.; Inukai, K.; Anai, M.; Fukushima, Y.; Kikuchi, M.; Yazaki, Y.; Oka, Y.; Asano, T. : 14-3-3 protein binds to insulin receptor substrate-1, one of the binding sites of which is in the phosphotyrosine binding domain. J. Biol. Chem. 272: 25267-25274, 1997. ; and

[6990] Powell, D. W.; Rane, M. J.; Chen, Q.; Singh, S.; McLeish, K. R. : Identification of 14-3-3-zeta as a protein kinase B/ Akt substrate. J. Biol. Chem. 277: 21639-21642, 2002.

[6991] Further studies establishing the function and utilities of YWHAZ are found in John Hopkins OMIM database record ID 601288, and in cited publications numbered 6379-6380, 4469, 1122 and 4192 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM_045261) is another VGAM43 host target gene. LRRN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRRN3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRN3 BINDING SITE, designated SEQ ID:34399, to the nucleotide sequence of VGAM43 RNA, herein designated VGAM RNA, also designated SEQ ID:2754.

[6992] Another function of VGAM43 is therefore inhibition of Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM_045261). Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRN3. SCDGF-B (Accession NM_025208) is another VGAM43 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:24881 and SEQ ID:26983 respectively, to the nucleotide sequence of VGAM43 RNA, herein designated VGAM RNA, also designated SEQ ID:2754.

[6993] Another function of VGAM43 is therefore inhibition of

SCDGF-B (Accession NM_025208). Accordingly, utilities of VGAM43 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCDGF-B. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 44 (VGAM44) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[6994] VGAM44 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM44 was detected is described hereinabove with reference to Figs. 1-8.

[6995] VGAM44 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[6996] VGAM44 gene encodes a VGAM44 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM44 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se-

quence of VGAM44 precursor RNA is designated SEQ ID:30, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:30 is located at position 117574 relative to the genome of Invertebrate Iridescent Virus 6.

[6997] VGAM44 precursor RNA folds onto itself, forming VGAM44 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[6998] An enzyme complex designated DICER COMPLEX, `dices` the VGAM44 folded precursor RNA into VGAM44 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM44 RNA is designated SEQ ID:2755, and is

provided hereinbelow with reference to the sequence listing part.

[6999] VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM44 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7000] VGAM44 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM44 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM44 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7001] The complementary binding of VGAM44 RNA, herein designated VGAM RNA, to host target binding sites on VGAM44 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM44 host target RNA into VGAM44 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7002] It is appreciated that VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM44 host target genes. The mRNA of each one of this plurality of VGAM44 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM44 RNA, herein designated VGAM

RNA, and which when bound by VGAM44 RNA causes inhibition of translation of respective one or more VGAM44 host target proteins.

[7003] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM44 gene, herein designated VGAM GENE, on one or more VGAM44 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7004] It is yet further appreciated that a function of VGAM44 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM44 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus

6. Specific functions, and accordingly utilities, of VGAM44 correlate with, and may be deduced from, the identity of the host target genes which VGAM44 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7005] Nucleotide sequences of the VGAM44 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM44 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM44 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM44 are further described hereinbelow with reference to Table 1.

[7006] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM44 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM44 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7007] As mentioned hereinabove with reference to Fig. 1, a function of VGAM44 gene, herein designated VGAM is inhibition of expression of VGAM44 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM44 correlate with, and may be deduced from, the identity of the target genes which VGAM44 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7008] LOC132671 (Accession NM_145263) is a VGAM44 host target gene. LOC132671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC132671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132671 BINDING SITE, designated SEQ ID:29778, to the nucleotide sequence of VGAM44 RNA, herein designated VGAM RNA, also designated SEQ ID:2755.

[7009] A function of VGAM44 is therefore inhibition of LOC132671 (Accession NM_145263). Accordingly, utilities of VGAM44 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132671. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 45 (VGAM45) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7010] VGAM45 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM45 was detected is described hereinabove with reference to Figs. 1–8.

[7011] VGAM45 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7012] VGAM45 gene encodes a VGAM45 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM45 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM45 precursor RNA is designated SEQ ID:31, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:31 is located at position 169711 relative to the genome of Invertebrate Iridescent Virus 6.

[7013] VGAM45 precursor RNA folds onto itself, forming VGAM45

folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7014] An enzyme complex designated DICER COMPLEX, `dices` the VGAM45 folded precursor RNA into VGAM45 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM45 RNA is designated SEQ ID:2756, and is provided hereinbelow with reference to the sequence listing part.

[7015] VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM45 host target RNA comprises three

regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7016] VGAM45 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM45 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM45 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target bind-

ing sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7017] The complementary binding of VGAM45 RNA, herein designated VGAM RNA, to host target binding sites on VGAM45 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM45 host target RNA into VGAM45 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7018] It is appreciated that VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM45 host target genes. The mRNA of each one of this plurality of VGAM45 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM45 RNA, herein designated VGAM RNA, and which when bound by VGAM45 RNA causes inhibition of translation of respective one or more VGAM45 host target proteins.

[7019] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM45 gene, herein designated VGAM GENE, on one or more VGAM45 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7020] It is yet further appreciated that a function of VGAM45 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM45 correlate with, and may be deduced from, the identity of the host target genes which VGAM45 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7021] Nucleotide sequences of the VGAM45 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM45 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM45 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM45 are further described hereinbelow with reference to Table 1.

[7022] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM45 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM45 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7023] As mentioned hereinabove with reference to Fig. 1, a function of VGAM45 gene, herein designated VGAM is inhibition of expression of VGAM45 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM45 correlate with, and may be deduced from, the identity of the target genes which VGAM45 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7024] Guanine Nucleotide Binding Protein (G protein), Alpha In-

hibiting Activity Polypeptide 3 (GNAI3, Accession NM_006496) is a VGAM45 host target gene. GNAI3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI3 BINDING SITE, designated SEQ ID:13237, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7025] A function of VGAM45 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 3 (GNAI3, Accession NM_006496), a gene which stimulates receptor regulated K⁺-channels. Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI3. The function of GNAI3 has been established by previous studies. Using a cDNA probe against a mouse/human somatic cell hybrid panel, Sparkes et al. (1987) mapped the alpha inhibiting polypeptide-3 of G protein to chromosome 1. See also Blatt et al. (1988). Alpha-3 cDNA codes for a protein of 340 amino acids (relative molecular weight 40,522), of

which the sequence is closely related to but distinct from that of alpha-2 (Itoh et al., 1988). By in situ hybridization, Wilkie et al. (1992) assigned the gene to 1p13. They assigned the corresponding gene to mouse chromosome 3 by study of restriction fragment length variation in an interspecific backcross. Baron et al. (1994) demonstrated that the Gnai3 gene in the hamster is less than 60 kb from the Ampd2 gene (OMIM Ref. No. 102771) with which it is coamplified in coformycin-resistant cells. The hamster Gnai3 gene did not contain sequences corresponding to the combined U6 snRNA and E protein pseudogene, previously identified within intron 7 of the human gene.

[7026] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7027] Baron, B.; Fernandez, M. A.; Toledo, F.; Le Roscouet, D.; Mayau, V.; Martin, N.; Buttin, G.; Debatisse, M. : The highly conserved Chinese hamster GNAI3 gene maps less than 60 kb from the AMPD2 gene and lacks the intronic U6 snRNA present in its human counterpart. Genomics 24: 288-294, 1994. ; and

[7028] Sparkes, R. S.; Cohn, V. H.; Mohandas, T.; Zollman, S.; Cire-Eversole, P.; Amatruda, T. T.; Reed, R. R.; Lochrie, M.

A.; Simon, M. I. : Mapping of genes encoding the subunits of guanine.

[7029] Further studies establishing the function and utilities of GNAI3 are found in John Hopkins OMIM database record ID 139370, and in cited publications numbered 3182, 474 and 2186 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274) is another VGAM45 host target gene. AKAP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP6 BINDING SITE, designated SEQ ID:10490, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7030] Another function of VGAM45 is therefore inhibition of A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP6. ARGBP2 (Accession NM_003603) is another VGAM45 host target gene.

ARGBP2 BINDING SITE1 and ARGBP2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ARGBP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARGBP2 BINDING SITE1 and ARGBP2 BINDING SITE2, designated SEQ ID:9658 and SEQ ID:22042 respectively, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7031] Another function of VGAM45 is therefore inhibition of ARGBP2 (Accession NM_003603). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARGBP2. FLJ20666 (Accession NM_017922) is another VGAM45 host target gene. FLJ20666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20666 BINDING SITE, designated SEQ ID:19580, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2756.

[7032] Another function of VGAM45 is therefore inhibition of FLJ20666 (Accession NM_017922). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20666. HMT1 HnRNP Methyltransferase-like 3 (*S. cerevisiae*) (HRMT1L3, Accession NM_019854) is another VGAM45 host target gene. HRMT1L3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HRMT1L3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRMT1L3 BINDING SITE, designated SEQ ID:21259, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7033] Another function of VGAM45 is therefore inhibition of HMT1 HnRNP Methyltransferase-like 3 (*S. cerevisiae*) (HRMT1L3, Accession NM_019854). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRMT1L3. KIAA0373 (Accession NM_014684) is another VGAM45 host target gene. KIAA0373 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0373 BINDING SITE, designated SEQ ID:16185, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7034] Another function of VGAM45 is therefore inhibition of KIAA0373 (Accession NM_014684). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0373. Zinc Finger RNA Binding Protein (ZFR, Accession NM_016107) is another VGAM45 host target gene. ZFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFR BINDING SITE, designated SEQ ID:18186, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7035] Another function of VGAM45 is therefore inhibition of Zinc

Finger RNA Binding Protein (ZFR, Accession NM_016107). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFR. LOC221271 (Accession XM_166307) is another VGAM45 host target gene. LOC221271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221271 BINDING SITE, designated SEQ ID:44122, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7036] Another function of VGAM45 is therefore inhibition of LOC221271 (Accession XM_166307). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221271. LOC221876 (Accession XM_168220) is another VGAM45 host target gene. LOC221876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC221876 BINDING SITE, designated SEQ ID:45079, to the nucleotide sequence of VGAM45 RNA, herein designated VGAM RNA, also designated SEQ ID:2756.

[7037] Another function of VGAM45 is therefore inhibition of LOC221876 (Accession XM_168220). Accordingly, utilities of VGAM45 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221876. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 46 (VGAM46) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7038] VGAM46 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM46 was detected is described hereinabove with reference to Figs. 1–8.

[7039] VGAM46 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[7040] VGAM46 gene encodes a VGAM46 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM46 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM46 precursor RNA is designated SEQ ID:32, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:32 is located at position 190087 relative to the genome of Invertebrate Iridescent Virus 6.

[7041] VGAM46 precursor RNA folds onto itself, forming VGAM46 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7042] An enzyme complex designated DICER COMPLEX, `dices` the VGAM46 folded precursor RNA into VGAM46 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM46 RNA is designated SEQ ID:2757, and is provided hereinbelow with reference to the sequence listing part.

[7043] VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM46 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7044] VGAM46 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM46 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of

each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM46 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7045] The complementary binding of VGAM46 RNA, herein designated VGAM RNA, to host target binding sites on VGAM46 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM46 host target RNA into VGAM46 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7046] It is appreciated that VGAM46 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM46 host target genes. The mRNA of each one of this plurality of VGAM46 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM46 RNA, herein designated VGAM RNA, and which when bound by VGAM46 RNA causes inhibition of translation of respective one or more VGAM46 host target proteins.

[7047] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM46 gene, herein designated VGAM GENE, on one or more VGAM46 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7048] It is yet further appreciated that a function of VGAM46 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM46 correlate with, and may be deduced from, the identity of the host target genes which VGAM46 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7049] Nucleotide sequences of the VGAM46 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM46 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM46 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM46 are further described hereinbelow with reference to Table 1.

[7050] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM46 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM46 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7051] As mentioned hereinabove with reference to Fig. 1, a function of VGAM46 gene, herein designated VGAM is inhibition of expression of VGAM46 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM46 correlate with, and may be deduced from, the identity of the target genes which VGAM46 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7052] COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_004376) is a VGAM46 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:10600, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7053] A function of VGAM46 is therefore inhibition of COX15

Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_004376). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Chemokine (C-X-C motif) Ligand 6 (granulocyte chemo-tactic protein 2) (CXCL6, Accession NM_002993) is another VGAM46 host target gene. CXCL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXCL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXCL6 BINDING SITE, designated SEQ ID:8884, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7054] Another function of VGAM46 is therefore inhibition of Chemokine (C-X-C motif) Ligand 6 (granulocyte chemo-tactic protein 2) (CXCL6, Accession NM_002993), a gene which is chemotactic for neutrophil granulocytes. Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXCL6. The function of CXCL6 has been established by previous studies. Rovai et al. (1997) cloned the

human GCP2 gene, as well as epithelial cell-derived neutrophil-activating peptide-78 (ENA78, or SCYB5; 600324). Both coding and noncoding portions of the GCP2 gene share very high nucleotide similarity to ENA78, except for the occurrence of a long interspersed sequence 5-prime of the GCP2 gene. The GCP2 gene encodes a propeptide of 114 amino acids. Despite 85% identity of the first 270 nucleotides 5-prime of the transcription start sites, GCP2 and the other CXC chemokine gene ENA78 showed cell-specific differences in regulation. Wuyts et al. (1997) synthesized and purified a human GCP2 protein of 75 amino acids. In vitro, synthetic GCP2 was an equally active chemoattractant for neutrophilic granulocytes as was natural 75-amino acid GCP2. Synthetic GCP2 did not stimulate eosinophil, monocyte, or lymphocyte chemotaxis. The authors showed that GCP2 binds to the chemokine receptors CXCR1 and CXCR2. In vivo studies in rabbit demonstrated that GCP2 is a potent inflammatory mediator.

[7055] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7056] Rovai, L. E.; Herschman, H. R.; Smith, J. B. : Cloning and characterization of the human granulocyte chemotactic

protein-2 gene. J. Immun. 158: 5257-5266, 1997. ; and

[7057] Wuyts, A.; van Osselaer, N.; Haelens, A.; Samson, I.; Herdewijn, P.; Ben-Baruch, A.; Oppenheim, J. J.; Proost, P.; van Damme, J. : Characterization of synthetic human granulocyte chemot.

[7058] Further studies establishing the function and utilities of CXCL6 are found in John Hopkins OMIM database record ID 138965, and in cited publications numbered 16 and 11961-165 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ephrin-B2 (EFNB2, Accession NM_004093) is another VGAM46 host target gene. EFNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EFNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNB2 BINDING SITE, designated SEQ ID:10298, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7059] Another function of VGAM46 is therefore inhibition of Ephrin-B2 (EFNB2, Accession NM_004093). Accordingly, utilities of VGAM46 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with EFNB2. Guanylate Binding Protein 1, Interferon-inducible, 67kDa (GBP1, Accession NM_002053) is another VGAM46 host target gene. GBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBP1 BINDING SITE, designated SEQ ID:7810, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7060] Another function of VGAM46 is therefore inhibition of Guanylate Binding Protein 1, Interferon-inducible, 67kDa (GBP1, Accession NM_002053), a gene which specifically binds guanylate nucleotides (GMP, GDP and GTP). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBP1. The function of GBP1 has been established by previous studies. Interferons are cytokines that have antiviral effects and inhibit tumor cell proliferation. They induce a large number of genes in their target cells, including those coding for the guanylate-binding proteins

(GBPs). GBPs are characterized by their ability to specifically bind guanine nucleotides (GMP, GDP, and GTP) and are distinguished from the GTP-binding proteins by the presence of 2 binding motifs rather than 3. Cheng et al. (1991) cloned the cDNAs for GBP1 (a 67-kD protein) and GBP2 (partial cDNA; 600412). Strehlow et al. (1994) identified the human GBP1 gene and showed that it contains 11 exons. By use of somatic cell hybrid DNAs, they mapped the gene to human chromosome 1. A mouse homolog of GBP1 has been mapped to the distal region of mouse chromosome 3 (Prochazka et al., 1985). Strehlow et al. (1994) also identified and partially characterized a third novel member of the family (GBP3; 600413) which shows significant sequence similarity to both GBP1 and GBP2. The putative window of embryo implantation in the human opens between days 19 to 24 of the menstrual cycle. A major challenge in the study of human reproduction is to identify the molecular signals that participate in the establishment of this critical receptive phase in the context of the natural cycle. Toward this goal, Kumar et al. (2001) analyzed human endometrial biopsies at various days of the menstrual cycle by mRNA differential display. They isolated several cDNAs representing genes that are

either up- or downregulated within the putative window of implantation. They identified one of these genes as GBP1, which possesses GTPase activity. Analysis of endometrial biopsies by Northern blot and RT-PCR demonstrated that GBP1 mRNA is specifically induced at the mid-secretory phase of the menstrual cycle. In situ hybridization analysis revealed that GBP1 mRNA expression is localized in the glandular epithelial cells as well as in the stroma in the immediate vicinity of the glands. The authors concluded that its unique expression overlapping the putative window of implantation suggests that GBP1 may serve as a useful marker of uterine receptivity in the human.

[7061] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7062] Cheng, Y.-S. E.; Patterson, C. E.; Staeheli, P. : Interferon-induced guanylate-binding proteins lack an N(T)KXD consensus motif and bind GMP in addition to GDP and GTP. *Molec. Cell. Biol.* 11: 4717-4725, 1991. ; and

[7063] Kumar, S.; Li, Q.; Dua, A.; Ying, Y.-K.; Bagchi, M. K.; Bagchi, I. C. : Messenger ribonucleic acid encoding interferon-inducible guanylate binding protein 1 is induced in

human endometri.

[7064] Further studies establishing the function and utilities of GBP1 are found in John Hopkins OMIM database record ID 600411, and in cited publications numbered 9865–9868 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MADS Box Transcription Enhancer Factor 2, Polypeptide A (myocyte enhancer factor 2A) (MEF2A, Accession NM_005587) is another VGAM46 host target gene. MEF2A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MEF2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF2A BINDING SITE, designated SEQ ID:12119, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7065] Another function of VGAM46 is therefore inhibition of MADS Box Transcription Enhancer Factor 2, Polypeptide A (myocyte enhancer factor 2A) (MEF2A, Accession NM_005587), a gene which binds a consensus sequence that regulates transcription. Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with MEF2A. The function of MEF2A has been established by previous studies. The process of differentiation from mesodermal precursor cells to myoblasts has led to the discovery of a variety of tissue-specific factors that regulate muscle gene expression. The myogenic basic helix-loop-helix proteins, including myoD (OMIM Ref. No. 159970), myogenin (OMIM Ref. No. 159980), MYF5 (OMIM Ref. No. 159990), and MRF4 (OMIM Ref. No. 159991) are 1 class of identified factors. A second family of DNA binding regulatory proteins is the myocyte-specific enhancer factor-2 (MEF2) family. Each of these proteins binds to the MEF2 target DNA sequence present in the regulatory regions of many, if not all, muscle-specific genes. The MEF2 genes are members of the MADS gene family (named for the yeast mating type-specific transcription factor MCM1, the plant homeotic genes 'agamous' and 'deficiens' and the human serum response factor SRF (OMIM Ref. No. 600589)), a family that also includes several homeotic genes and other transcription factors, all of which share a conserved DNA-binding domain. Pollock and Treisman (1991) cloned a cDNA for MEF2A, which they designated as a member of the RSRF (related to serum response fac-

tor) family. They also described the protein's DNA binding properties and its potential role in regulation of growth factor-inducible and muscle specific sequences. MEF2A cDNAs were also obtained by Yu et al. (1992), who screened an expression library of primary human skeletal myocytes from vastus lateralis with a DNA probe containing multiple copies of the MEF2 binding sequence. The mRNA is ubiquitously expressed, with highest levels found in skeletal muscle, heart, and brain. Several alternative splice variants of MEF2A were identified that were predicted to encode different protein products. Using immunofluorescence, MEF2A protein was detected in the nuclei of skeletal and cardiac muscle cells. Hobson et al. (1995) mapped the MEF2A gene using somatic cell hybrid panel DNAs including deletion or derivative chromosome cell lines and regionalized it to 15q26 by fluorescence in situ hybridization (FISH) with a YAC shown to contain MEF2A. Mouse Mef2A was mapped by Martin et al. (1994) to chromosome 7. Suzuki et al. (1996) mapped the MEF2A gene to 15q26 by FISH. They isolated and mapped a partially processed pseudogene (OMIM Ref. No. MEF2AP) to 1q24-q25 by FISH. Animal model experiments lend further support to the function of MEF2A. Naya et al. (2002)

generated mice deficient in Mef2a, the predominant Mef2 gene expressed in postnatal cardiac muscle. Most mice lacking Mef2a died suddenly within the first week of life and exhibited pronounced dilation of the right ventricle, myofibrillar fragmentation, mitochondrial disorganization, and activation of a fetal cardiac gene program. The few Mef2a null mice that survived to adulthood also showed a deficiency of cardiac mitochondria and susceptibility to sudden death.

[7066] It is appreciated that the abovementioned animal model for MEF2A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7067] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7068] Pollock, R.; Treisman, R. : Human SRF-related proteins: DNA-binding properties and potential regulatory targets. *Genes Dev.* 5: 2327-2341, 1991. ; and

[7069] Suzuki, E.; Lowry, J.; Sonoda, G.; Testa, J. R.; Walsh, K. : Structures and chromosome locations of the human MEF2A gene and a pseudogene MEF2AP. *Cytogenet. Cell Genet.* 73: 244-249, 1996.

[7070] Further studies establishing the function and utilities of MEF2A are found in John Hopkins OMIM database record ID 600660, and in cited publications numbered 8293–8301 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM_002709) is another VGAM46 host target gene. PPP1CB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1CB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1CB BINDING SITE, designated SEQ ID:8559, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7071] Another function of VGAM46 is therefore inhibition of Protein Phosphatase 1, Catalytic Subunit, Beta Isoform (PPP1CB, Accession NM_002709), a gene which is the catalytic subunit of protein phosphatase 1. Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1CB. The function of PPP1CB has been established by

previous studies. Protein phosphatase 1 (PP1) is one of 4 major serine/threonine-specific protein phosphatases involved in the dephosphorylation of a variety of proteins. These enzymes work in opposition to the protein kinases to control the level of phosphorylation. PP1 has 3 catalytic subunits, designated alpha (OMIM Ref. No. 176875), beta, and gamma. Barker et al. (1994) isolated a cDNA for PP1 beta (symbolized PPP1CB) from a teratocarcinoma library. Three different PPP1CB mRNAs were seen on Northern blots corresponding to alternate splicing variants. The 3-prime noncoding region of PPP1CB was approximately 90% conserved between man and rodents, suggesting that this region may have functional importance. Barker et al. (1994) assigned the gene for human PPP1CB to chromosome 2 using somatic cell hybrid DNAs and further localized it to 2p23 by fluorescence in situ hybridization. Saadat et al. (1994) confirmed the human map position as 2p23 and showed that rodent homologs mapped to rat 6q21-q23 and mouse 12D

[7072] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7073] Barker, H. M.; Brewis, N. D.; Street, A. J.; Spurr, N. K.; Co-

hen, P. T. W. : Three genes for protein phosphatase 1 map to different human chromosomes: sequence, expression and gene localisation of protein serine/threonine phosphatase 1 beta (PPP1CB). Biochim. Biophys. Acta 1220: 212-218, 1994. ; and

[7074] Saadat, M.; Kakinoki, Y.; Mizuno, Y.; Kikuchi, K.; Yoshida, M. C. : Chromosomal localization of human, rat, and mouse protein phosphatase type 1 beta catalytic subunit genes (PPP1CB) by.

[7075] Further studies establishing the function and utilities of PPP1CB are found in John Hopkins OMIM database record ID 600590, and in cited publications numbered 10217-10218 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Basic, Immunoglobulin-like Variable Motif Containing (BIVM, Accession NM_017693) is another VGAM46 host target gene. BIVM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BIVM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIVM BINDING SITE, designated SEQ ID:19256, to the nucleotide sequence of VGAM46

RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7076] Another function of VGAM46 is therefore inhibition of Basic, Immunoglobulin-like Variable Motif Containing (BIVM, Accession NM_017693). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIVM. Cadherin-like 26 (CDH26, Accession NM_021810) is another VGAM46 host target gene. CDH26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH26 BINDING SITE, designated SEQ ID:22373, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7077] Another function of VGAM46 is therefore inhibition of Cadherin-like 26 (CDH26, Accession NM_021810). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH26. FLJ10961 (Accession XM_032826) is another VGAM46 host target gene. FLJ10961 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10961 BINDING SITE, designated SEQ ID:31777, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7078] Another function of VGAM46 is therefore inhibition of FLJ10961 (Accession XM_032826). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10961. HTMP10 (Accession NM_033207) is another VGAM46 host target gene. HTMP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTMP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTMP10 BINDING SITE, designated SEQ ID:27051, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7079] Another function of VGAM46 is therefore inhibition of

HTMP10 (Accession NM_033207). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTMP10. KIAA0471 (Accession NM_014857) is another VGAM46 host target gene. KIAA0471 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0471, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0471 BINDING SITE, designated SEQ ID:16916, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7080] Another function of VGAM46 is therefore inhibition of KIAA0471 (Accession NM_014857). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0471. KIAA1493 (Accession XM_034415) is another VGAM46 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32090, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7081] Another function of VGAM46 is therefore inhibition of KIAA1493 (Accession XM_034415). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. KIAA1634 (Accession XM_032749) is another VGAM46 host target gene. KIAA1634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1634 BINDING SITE, designated SEQ ID:31749, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7082] Another function of VGAM46 is therefore inhibition of KIAA1634 (Accession XM_032749). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1634. KIAA1877 (Accession XM_038616) is another

VGAM46 host target gene. KIAA1877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1877 BINDING SITE, designated SEQ ID:32888, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7083] Another function of VGAM46 is therefore inhibition of KIAA1877 (Accession XM_038616). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1877. Mal, T-cell Differentiation Protein 2 (MAL2, Accession NM_052886) is another VGAM46 host target gene. MAL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAL2 BINDING SITE, designated SEQ ID:27470, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7084] Another function of VGAM46 is therefore inhibition of Mal, T-cell Differentiation Protein 2 (MAL2, Accession NM_052886). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAL2. SB52 (Accession NM_138335) is another VGAM46 host target gene. SB52 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SB52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SB52 BINDING SITE, designated SEQ ID:28735, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7085] Another function of VGAM46 is therefore inhibition of SB52 (Accession NM_138335). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SB52. LOC150848 (Accession XM_097959) is another VGAM46 host target gene. LOC150848 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150848 BINDING SITE, designated SEQ ID:41262, to the nucleotide sequence of VGAM46 RNA, herein designated VGAM RNA, also designated SEQ ID:2757.

[7086] Another function of VGAM46 is therefore inhibition of LOC150848 (Accession XM_097959). Accordingly, utilities of VGAM46 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150848. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 47 (VGAM47) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7087] VGAM47 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM47 was detected is described hereinabove with reference to Figs. 1–8.

[7088] VGAM47 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM47 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7089] VGAM47 gene encodes a VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM47 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM47 precursor RNA is designated SEQ ID:33, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:33 is located at position 25939 relative to the genome of Invertebrate Iridescent Virus 6.

[7090] VGAM47 precursor RNA folds onto itself, forming VGAM47 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7091] An enzyme complex designated DICER COMPLEX, `dices` the VGAM47 folded precursor RNA into VGAM47 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM47 RNA is designated SEQ ID:2758, and is provided hereinbelow with reference to the sequence listing part.

[7092] VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM47 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7093] VGAM47 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM47 RNA is an accurate or a partial in-

versed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM47 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7094] The complementary binding of VGAM47 RNA, herein designated VGAM RNA, to host target binding sites on VGAM47 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM47 host target RNA into VGAM47 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7095] It is appreciated that VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM47 host target genes. The mRNA of each one of this plurality of VGAM47 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM47 RNA, herein designated VGAM RNA, and which when bound by VGAM47 RNA causes inhibition of translation of respective one or more VGAM47 host target proteins.

[7096] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM47 gene, herein designated VGAM GENE, on one or more VGAM47 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7097] It is yet further appreciated that a function of VGAM47 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM47 correlate with, and may be deduced from, the identity of the host target genes which VGAM47 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7098] Nucleotide sequences of the VGAM47 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM47 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM47 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM47 are further described hereinbelow with reference to Table 1.

[7099] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM47 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM47 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7100] As mentioned hereinabove with reference to Fig. 1, a function of VGAM47 gene, herein designated VGAM is inhibition of expression of VGAM47 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM47 correlate with, and may be deduced from, the identity of the target genes which VGAM47 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7101] Aspartate Beta-hydroxylase (ASPH, Accession NM_032466) is a VGAM47 host target gene. ASPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASPH BINDING SITE, designated SEQ ID:26223, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7102] A function of VGAM47 is therefore inhibition of Aspartate

Beta-hydroxylase (ASPH, Accession NM_032466), a gene which specifically hydroxylates the beta carbon of aspartic acid or asparagine residues in certain epidermal growth factor (EGF)-like domains of a number of proteins. Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASPH. The function of ASPH has been established by previous studies. In hepatocellular carcinoma (HCC; 114550), one of the most prevalent tumors in the world which occurs with especially high frequency in sub-Saharan Africa and the Far East, a specific antigen is highly expressed; it is highly expressed also in cholangiocarcinomas. Lavaissiere et al. (1996) reported cDNA cloning of the human gene encoding this antigen, aspartyl(asparaginyl)-beta-hydroxylase (symbolized HAAH by them), and demonstrated that in these tumor lines it is expressed in an enzymatically active form. The gene encodes a deduced 744-amino acid polypeptide with high homology (81%) to the bovine gene (Jia et al., 1992). Lavaissiere et al. (1996) found that their cDNA human sequence was 99% homologous to the sequence for ASPH reported by Koriath et al. (1994), differing only at amino acid residues 565 (tyr to ile), 575 (trp-trp-thr to cys-gly),

585 (asp to gln), and 709 (arg to lys). They noted also a silent TCG-to-TCA transition at peptide residue 161.

Lavaissiere et al. (1996) speculated about the possible relationship of the malignant phenotype of regulated aspartyl/asparaginyl-beta-hydroxylation in EGF-like domains of proteins such as the mammalian Notch homologs (e.g., 190198, 600275, and 600276), which are known to be involved in cell differentiation and whose cytoplasmic domains have been shown to be oncogenic. By screening a heart cDNA library, followed by RT-PCR, Lim et al. (2000) isolated cDNAs encoding the 225-amino acid junctin protein and a 210-amino acid isoform. The authors noted that a 73-residue stretch in junctin has a completely matched region in the ASPH protein. Southern blot analysis indicated that junctin and ASPH exist as a single-copy gene. Northern blot analysis revealed expression of 3.0- and 4.2-kb transcripts in cardiac and skeletal muscle; expression was higher in skeletal muscle. SDS-PAGE analysis of the translated cDNAs showed expression of 26- and 28-kD proteins. By screening a skeletal muscle cDNA library with a dog junctin probe, Treves et al. (2000) identified cDNAs encoding human junctin and junctate. Sequence analysis predicted that junctate, a 299-amino

acid protein, shares the first 93 amino acids of the long isoform of junctin (and, partially, of ASPH), whereas its 64 C-terminal residues are identical to the central region of ASPH. Northern blot analysis detected a 2.6-kb transcript in heart, brain, pancreas, placenta, lung, liver, kidney, and skeletal muscle; highest levels were in heart, brain, and pancreas, and lowest levels were in skeletal muscle. In contrast, junctin was expressed only in cardiac and skeletal muscle. Southern blot and PCR analyses indicated that ASPH, junctin, and junctate are splice variants of the same gene; ASPH uses exons 1, 3, 5, and 8 through 16, whereas junctin uses exons 2, 3, 5, and 6, and junctate uses exons 2 through 5 and 8 through 16. Fluorescence microscopy showed junctate expression in sarco(endo)plasmic reticulum membranes. Immunoblot analysis indicated that junctate is expressed as a 32-kD protein in kidney microsomes. Binding analysis determined that junctate binds calcium with high capacity and moderate affinity.

[7103] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7104] Lavaissiere, L.; Jia, S.; Nishiyama, M.; de la Monte, S.; Stern, A. M.; Wands, J. R.; Friedman, P. A. : Overexpression

of human aspartyl(asparaginyl)-beta-hydroxylase in hepatocellular carcinoma and cholangiocarcinoma. J. Clin. Invest. 98: 1313-1323, 1996. ; and

[7105] Treves, S.; Feriotto, G.; Moccagatta, L.; Gambari, R.; Zorzato, F. : Molecular cloning, expression, functional characterization, chromosomal localization, and gene structure of junctate.

[7106] Further studies establishing the function and utilities of ASPH are found in John Hopkins OMIM database record ID 600582, and in cited publications numbered 10187-10193 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM_020390) is another VGAM47 host target gene. EIF5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5A2 BINDING SITE, designated SEQ ID:21659, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7107] Another function of VGAM47 is therefore inhibition of Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM_020390). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5A2. RP42 (Accession NM_020640) is another VGAM47 host target gene. RP42 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP42 BINDING SITE, designated SEQ ID:21801, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7108] Another function of VGAM47 is therefore inhibition of RP42 (Accession NM_020640), a gene which not clear yet. Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP42. The function of RP42 has been established by previous studies. In a systematic search for genes expressed in proliferating neuroblasts whose human orthologs map to susceptibility loci for autism (OMIM Ref. No. 209850), Mas et al. (2000) isolated a novel mouse

gene, which they designated RP42. They obtained the human homolog by combining contigs of human ESTs and RT-PCR of human embryonic mRNAs. The deduced human and mouse RP42 proteins contain 259 amino acids and differ by only 2 residues. They show 30 to 36% overall sequence identity to an *S. pombe* and a *C. elegans* protein, suggesting that the RP42 protein has an important cellular function. Northern blot analysis in the mouse embryo demonstrated expression of 2 transcripts, with the larger transcript reaching peak expression from E11 to E15, and the smaller transcript showing high expression from E7 to E15, indicating developmentally regulated expression, which was found particularly in proliferating neuroblasts. In mouse adult tissues, 3 transcripts were expressed in testis, kidney, liver, skeletal muscle, and heart, with weaker expression in brain. Northern blot analysis of adult human tissues detected 2 RP42 transcripts of approximately 3.7 and 2.7 kb at lower levels of expression than in mouse. RT-PCR showed that RP42 is expressed in the human embryo telencephalon Mas et al. (2000) identified the human RP42 sequence in a cluster of embryonic neuronally expressed genes on a PAC mapping to 6q16, making it a candidate gene for the susceptibility autism locus

previously assigned to this region

[7109] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7110] Mas, C.; Bourgeois, F.; Bulfone, A.; Levacher, B.; Mugnier, C.; Simonneau, M. : Cloning and expression analysis of a novel gene, RP42, mapping to an autism susceptibility locus on 6q16. Genomics 65: 70–74, 2000. ; and

[7111] Mas, C.; Bourgeois, F.; Bulfone, A.; Levacher, B.; Mugnier, C.; Simonneau, M. : Cloning and expression analysis of a novel gene, RP42, mapping to an autism susceptibility locus on 6q16. Ge.

[7112] Further studies establishing the function and utilities of RP42 are found in John Hopkins OMIM database record ID 605905, and in cited publications numbered 739 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor, Arginine/serine-rich 2 (SFRS2, Accession XM_036785) is another VGAM47 host target gene. SFRS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SFRS2 BINDING SITE, designated SEQ ID:32504, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7113] Another function of VGAM47 is therefore inhibition of Splicing Factor, Arginine/serine-rich 2 (SFRS2, Accession XM_036785), a gene which is necessary for the splicing of pre-mrna. Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS2. The function of SFRS2 has been established by previous studies. Fu and Maniatis (1992) isolated a human cDNA termed pre-mRNA splicing factor SC35, or SFRS2, that is required for spliceosome assembly. The predicted protein contains a ribonucleoprotein (RNP)-type RNA-binding motif and a carboxyl-terminal serine/arginine-rich (SR) domain. Wang et al. (2001) reported that Cre-mediated conditional deletion of the prototypical SR protein Sc35 in mouse thymus caused a defect in T-cell maturation. Deletion of Sc35 altered alternative splicing of CD45 (OMIM Ref. No. 151460), a receptor tyrosine phosphatase regulated by differential splicing during thymocyte development and activation.

[7114] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

[7115] Fu, X.-D.; Maniatis, T. : Isolation of a complementary DNA that encodes the mammalian splicing factor SC35. Science 256: 535-538, 1992. ; and

[7116] Wang, H.-Y.; Xu, X.; Ding, J.-H.; Bermingham, J. R., Jr.; Fu, X.-D. : SC35 plays a role in T cell development and alternative splicing of CD45. Molec. Cell 7: 331-342, 2001.

[7117] Further studies establishing the function and utilities of SFRS2 are found in John Hopkins OMIM database record ID 600813, and in cited publications numbered 713 and 7140-7142 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TSG (Accession NM_020648) is another VGAM47 host target gene. TSG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSG BINDING SITE, designated SEQ ID:21811, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7118] Another function of VGAM47 is therefore inhibition of TSG

(Accession NM_020648). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSG. KIAA1332 (Accession XM_048774) is another VGAM47 host target gene. KIAA1332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1332 BINDING SITE, designated SEQ ID:35258, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7119] Another function of VGAM47 is therefore inhibition of KIAA1332 (Accession XM_048774). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1332. KIAA1912 (Accession XM_055636) is another VGAM47 host target gene. KIAA1912 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1912 BINDING SITE, designated SEQ ID:36313, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7120] Another function of VGAM47 is therefore inhibition of KIAA1912 (Accession XM_055636). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1912. LOC127534 (Accession XM_060532) is another VGAM47 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37172, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7121] Another function of VGAM47 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC146880 (Accession XM_085627) is an-

other VGAM47 host target gene. LOC146880 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146880, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146880 BINDING SITE, designated SEQ ID:38259, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7122] Another function of VGAM47 is therefore inhibition of LOC146880 (Accession XM_085627). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146880. LOC221656 (Accession XM_166418) is another VGAM47 host target gene. LOC221656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221656 BINDING SITE, designated SEQ ID:44294, to the nucleotide sequence of VGAM47 RNA, herein designated VGAM RNA, also designated SEQ ID:2758.

[7123] Another function of VGAM47 is therefore inhibition of LOC221656 (Accession XM_166418). Accordingly, utilities of VGAM47 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221656. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 48 (VGAM48) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7124] VGAM48 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM48 was detected is described hereinabove with reference to Figs. 1–8.

[7125] VGAM48 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7126] VGAM48 gene encodes a VGAM48 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM48

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM48 precursor RNA is designated SEQ ID:34, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:34 is located at position 168080 relative to the genome of Invertebrate Iridescent Virus 6.

[7127] VGAM48 precursor RNA folds onto itself, forming VGAM48 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7128] An enzyme complex designated DICER COMPLEX, `dices` the VGAM48 folded precursor RNA into VGAM48 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 46%) nucleotide sequence of VGAM48 RNA is designated SEQ ID:2759, and is provided hereinbelow with reference to the sequence listing part.

- [7129] VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM48 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.
- [7130] VGAM48 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM48 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host tar-

get binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM48 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7131] The complementary binding of VGAM48 RNA, herein designated VGAM RNA, to host target binding sites on VGAM48 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM48 host target RNA into VGAM48 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7132] It is appreciated that VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM48 host target genes. The mRNA of each one of this plurality of VGAM48 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM48 RNA, herein designated VGAM RNA, and which when bound by VGAM48 RNA causes inhibition of translation of respective one or more VGAM48 host target proteins.

[7133] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM48 gene, herein designated VGAM GENE, on one or more VGAM48 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7134] It is yet further appreciated that a function of VGAM48 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM48 correlate with, and may be deduced from, the identity of the host target genes which VGAM48 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7135] Nucleotide sequences of the VGAM48 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM48 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM48 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM48 are further described hereinbelow with reference to Table 1.

[7136] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM48 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM48 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7137] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM48 gene, herein designated VGAM is inhibition of expression of VGAM48 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM48 correlate with, and may be deduced from, the identity of the target genes which VGAM48 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7138] Chloride Channel 5 (nephrolithiasis 2, X-linked, Dent disease) (CLCN5, Accession NM_000084) is a VGAM48 host target gene. CLCN5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLCN5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLCN5 BINDING SITE, designated SEQ ID:5535, to the nucleotide sequence of VGAM48 RNA, herein designated VGAM RNA, also designated SEQ ID:2759.

[7139] A function of VGAM48 is therefore inhibition of Chloride Channel 5 (nephrolithiasis 2, X-linked, Dent disease) (CLCN5, Accession NM_000084), a gene which may interfere in renal tubular function. Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with CLCN5. The function of CLCN5 has been established by previous studies. Lloyd et al. (1996) found mutations in the CLCN5 gene in each of 11 kindreds with different renal tubular disorders complicated by kidney stone formation (nephrolithiasis): Dent disease, X-linked recessive nephrolithiasis (OMIM Ref. No. 310468), and X-linked recessive hypophosphatemic rickets (OMIM Ref. No. 307800). There are clearly 2 or more forms of X-linked recessive hypophosphatemia, because one form has already been identified as due to mutations in the gene variously symbolized HYP or PEX, an X-linked phosphate regulating gene with homologies to endopeptidases (see, OMIM Ref. No., for example, 307800.0001). Lloyd et al. (1996) found that heterologous expression of wildtype CLCN5 in *Xenopus* oocytes yielded outwardly rectifying chloride currents, which were either abolished or markedly reduced by the mutations they found in the gene in these families. Lloyd et al. (1996) found Dent disease associated with the mutations W279X (300008.0001), R648X (300008.0002), L200R (300008.0003), S529P (300008.0004), 2 microdeletions, and 2 donor splice site mutations; X-linked nephrolithia-

sis was associated with R704X (300008.0005) and G506E (300008.0006); and X-linked hypophosphatemia was associated with S244L (300008.0007). All the disease-causing missense mutations were confined to the predicted transmembrane domains. In addition, the R648X and R704X mutations, which predicted a loss of 142 amino acids from the cytoplasmic C-terminus, had deleted domain D13, which is conserved in all eukaryotic chloride channel proteins. The donor splice site mutations, which were associated with a loss of exon 5, led to an in-frame deletion of the predicted transmembrane domain D2. An annual urinary screening program of Japanese children above 3 years of age identified a progressive proximal renal tubular disorder characterized by low molecular weight proteinuria, hypercalciuria, and nephrocalcinosis (Igarashi et al., 1995). Some children additionally demonstrated hematuria, glycosuria, aminoaciduria, impaired urinary concentrating ability, and mild decrease in creatinine clearance. The disease occurred predominantly in males and had been reported to be familial. Although the disorder was similar to Dent disease, notable differences were the lack of rickets or renal failure in the Japanese children. Lloyd et al. (1997) investigated 4 unrelated

Japanese kindreds with this tubulopathy and identified 4 different CLCN5 mutations (2 OMIM Ref. No. 300008.0008). Mutational screening of CLCN5 by SSCP analysis was predicted to help supplement the clinical evaluation of the annual urinary screening program for this disorder. Animal model experiments lend further support to the function of CLCN5. Piwon et al. (2000) created an animal model of Dent disease by targeted disruption of the *Clcn5* gene in mice. *Clcn5* $-/-$ mice had proteinuria due to strong reduction of apical proximal tubular endocytosis. Both receptor-mediated and fluid-phase endocytosis were affected, and the internalization of the apical transporters NaPi2 and NHE3 (OMIM Ref. No. 182307) was slowed. At steady state, however, both proteins were redistributed from the plasma membrane to intracellular vesicles. Piwon et al. (2000) postulated that this may have been caused by an increased stimulation of luminal parathyroid hormone (PTH; 168450) receptors (see OMIM Ref. No. 168468) owing to the observed decreased tubular endocytosis of PTH. The rise in luminal PTH concentration should also stimulate the hydroxylation of 25-hydroxy vitamin D3 to the active hormone. However, this would be counteracted by a urinary loss of the pre-

cursor 25-hydroxy vitamin D3. The balance between these opposing effects, both of which are secondary to the defect in proximal tubular endocytosis, probably determines whether there will be hypercalciuria and kidney stones. Piwon et al. (2000) showed that CLC5 is crucial for efficient endocytosis in the proximal tubule. CLC5 was the first intracellular chloride channel for which a role in vesicle trafficking was established. Piwon et al. (2000) argued that their mouse model strongly suggests that alterations in hormones involved in calcium homeostasis, and hyperphosphaturia and hypocalciuria, are indirect effects of defective apical endocytosis of PTH and 25-hydroxy D3; this may explain how a defect in a chloride channel could lead to kidney stones.

[7140] It is appreciated that the abovementioned animal model for CLCN5 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7141] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7142] Igarashi, T.; Hayakawa, H.; Shiraga, H.; Kawato, H.; Yan, K.; Kawaguchi, H.; Yamanake, T.; Tsuchida, S.; Akagi, K. :

Hypercalciuria and nephrocalcinosis in patients with idiopathic low molecular weight proteinuria in Japan: is the disease identical to Dent's disease in the United Kingdom? Nephron. 69: 242–247, 1995. ; and

[7143] Lloyd, S. E.; Gunther, W.; Pearce, S. H. S.; Thomson, A.; Bianchi, M. L.; Bosio, M.; Craig, I. W.; Fisher, S. E.; Scheinman, S. J.; Wrong, O.; Jentsch, T. J.; Thakker, R. V. : Character.

[7144] Further studies establishing the function and utilities of CLCN5 are found in John Hopkins OMIM database record ID 300008, and in cited publications numbered 6569–6583 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM48 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31079, to the nucleotide sequence of VGAM48 RNA, herein designated VGAM RNA, also designated SEQ ID:2759.

[7145] Another function of VGAM48 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. KIAA1383 (Accession XM_045859) is another VGAM48 host target gene. KIAA1383 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1383, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1383 BINDING SITE, designated SEQ ID:34583, to the nucleotide sequence of VGAM48 RNA, herein designated VGAM RNA, also designated SEQ ID:2759.

[7146] Another function of VGAM48 is therefore inhibition of KIAA1383 (Accession XM_045859). Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1383. LOC219722 (Accession XM_167593) is another VGAM48 host target gene. LOC219722 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219722, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219722 BINDING SITE, designated SEQ ID:44708, to the nucleotide sequence of VGAM48 RNA, herein designated VGAM RNA, also designated SEQ ID:2759.

[7147] Another function of VGAM48 is therefore inhibition of LOC219722 (Accession XM_167593). Accordingly, utilities of VGAM48 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219722. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 49 (VGAM49) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7148] VGAM49 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM49 was detected is described hereinabove with reference to Figs. 1–8.

[7149] VGAM49 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7150] VGAM49 gene encodes a VGAM49 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM49 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM49 precursor RNA is designated SEQ ID:35, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:35 is located at position 104443 relative to the genome of Invertebrate Iridescent Virus 6.

[7151] VGAM49 precursor RNA folds onto itself, forming VGAM49 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide

sequence of the second half thereof.

[7152] An enzyme complex designated DICER COMPLEX, `dices` the VGAM49 folded precursor RNA into VGAM49 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM49 RNA is designated SEQ ID:2760, and is provided hereinbelow with reference to the sequence listing part.

[7153] VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM49 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7154] VGAM49 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM49 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM49 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM49 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7155] The complementary binding of VGAM49 RNA, herein designated VGAM RNA, to host target binding sites on VGAM49 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM49 host tar-

get RNA into VGAM49 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7156] It is appreciated that VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM49 host target genes. The mRNA of each one of this plurality of VGAM49 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM49 RNA, herein designated VGAM RNA, and which when bound by VGAM49 RNA causes inhibition of translation of respective one or more VGAM49 host target proteins.

[7157] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM49 gene, herein designated VGAM GENE, on one or more VGAM49 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and

Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7158] It is yet further appreciated that a function of VGAM49 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM49 correlate with, and may be deduced from, the identity of the host target genes which VGAM49 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7159] Nucleotide sequences of the VGAM49 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM49 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM49 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM49 are further described hereinbelow with reference to Table 1.

[7160] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM49 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM49 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7161] As mentioned hereinabove with reference to Fig. 1, a function of VGAM49 gene, herein designated VGAM is inhibition of expression of VGAM49 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM49 correlate with, and may be deduced from, the identity of the target genes which VGAM49 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7162] Immunoglobulin J Polypeptide, Linker Protein For Immunoglobulin Alpha and Mu Polypeptides (IGJ, Accession NM_144646) is a VGAM49 host target gene. IGJ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGJ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGJ BIND-

ING SITE, designated SEQ ID:29472, to the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7163] A function of VGAM49 is therefore inhibition of Immunoglobulin J Polypeptide, Linker Protein For Immunoglobulin Alpha and Mu Polypeptides (IGJ, Accession NM_144646), a gene which serves to link two monomer units of either igm or iga and also helps to bind these immunoglobulins to secretory components. Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGJ. The function of IGJ has been established by previous studies. J chain is a 137-amino acid protein that is synthesized in B lymphocytes and serves 2 known functions: linking immunoglobulin monomers (IgM to pentamers, IgA to dimers) and binding these immunoglobulins to secretory component (Koshland, 1985). Using probes from J chain clones, Max et al. (1986) assigned the J chain gene to 4q21 by Southern analysis of somatic cell hybrids and by in situ hybridization. This band is the site of translocations with chromosome 11 in some acute lymphocytic leukemias. In the mouse, JCH maps to chromosome 5 which carries 4 other genes that are also on hu-

man no. 4 (PGM2, PEPS, ALB, and AFP). Max et al. (1986) also discovered genetic variation in the number of repeats of a 27-bp sequence that is tandemly reduplicated 5-prime of the human J chain gene. They suggested that this polymorphism may be 'useful in genetic linkage studies in a region of chromosome 4 heretofore relatively barren of markers definitively localized to a particular sub-band.' (The OMIM Ref. No. 146970, 147010, 147230 for the J region genes of kappa, heavy and lambda chains, respectively.)

- [7164] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [7165] Koshland, M. E. : The coming of age of the immunoglobulin J chain. Annu. Rev. Immun. 3: 425-453, 1985. ; and
- [7166] Max, E. E.; McBride, O. W.; Morton, C. C.; Robinson, M. A. : Human J chain gene: chromosomal localization and associated restriction fragment length polymorphisms. Proc. Nat. Acad. Sci.
- [7167] Further studies establishing the function and utilities of IGJ are found in John Hopkins OMIM database record ID 147790, and in cited publications numbered 11593-11594 listed in the bibliography section hereinbe-

low, which are also hereby incorporated by reference. ATP6M8-9 (Accession NM_005765) is another VGAM49 host target gene. ATP6M8-9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6M8-9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6M8-9 BINDING SITE, designated SEQ ID:12327, to the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7168] Another function of VGAM49 is therefore inhibition of ATP6M8-9 (Accession NM_005765). Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6M8-9. KIAA0447 (Accession XM_049733) is another VGAM49 host target gene. KIAA0447 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35490, to the

nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7169] Another function of VGAM49 is therefore inhibition of KIAA0447 (Accession XM_049733). Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. MGC11352 (Accession XM_035941) is another VGAM49 host target gene. MGC11352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11352 BINDING SITE, designated SEQ ID:32356, to the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7170] Another function of VGAM49 is therefore inhibition of MGC11352 (Accession XM_035941). Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11352. LOC136015 (Accession XM_072440) is another VGAM49 host target gene. LOC136015 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC136015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC136015 BINDING SITE, designated SEQ ID:37500, to the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7171] Another function of VGAM49 is therefore inhibition of LOC136015 (Accession XM_072440). Accordingly, utilities of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC136015. LOC154788 (Accession XM_098607) is another VGAM49 host target gene. LOC154788 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154788, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154788 BINDING SITE, designated SEQ ID:41725, to the nucleotide sequence of VGAM49 RNA, herein designated VGAM RNA, also designated SEQ ID:2760.

[7172] Another function of VGAM49 is therefore inhibition of LOC154788 (Accession XM_098607). Accordingly, utilities

of VGAM49 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154788. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 50 (VGAM50) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7173] VGAM50 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM50 was detected is described hereinabove with reference to Figs. 1–8.

[7174] VGAM50 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7175] VGAM50 gene encodes a VGAM50 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM50 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM50 precursor RNA is designated SEQ ID:36, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:36 is located at position 92898 relative to the genome of Invertebrate Iridescent Virus 6.

[7176] VGAM50 precursor RNA folds onto itself, forming VGAM50 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7177] An enzyme complex designated DICER COMPLEX, `dices` the VGAM50 folded precursor RNA into VGAM50 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM50 RNA is designated SEQ ID:2761, and is

provided hereinbelow with reference to the sequence listing part.

[7178] VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM50 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[7179] VGAM50 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM50 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM50 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7180] The complementary binding of VGAM50 RNA, herein designated VGAM RNA, to host target binding sites on VGAM50 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM50 host target RNA into VGAM50 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7181] It is appreciated that VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM50 host target genes. The mRNA of each one of this plurality of VGAM50 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM50 RNA, herein designated VGAM

RNA, and which when bound by VGAM50 RNA causes inhibition of translation of respective one or more VGAM50 host target proteins.

[7182] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM50 gene, herein designated VGAM GENE, on one or more VGAM50 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7183] It is yet further appreciated that a function of VGAM50 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM50 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM50 correlate with, and may be deduced from, the identity of the host target genes which VGAM50 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7184] Nucleotide sequences of the VGAM50 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM50 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM50 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM50 are further described hereinbelow with reference to Table 1.

[7185] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM50 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM50 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7186] As mentioned hereinabove with reference to Fig. 1, a function of VGAM50 gene, herein designated VGAM is inhibition of expression of VGAM50 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM50 correlate with, and may be deduced from, the identity of the target genes which VGAM50 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7187] Inositol Polyphosphate-5-phosphatase, 75kDa (INPP5B, Accession XM_170949) is a VGAM50 host target gene. INPP5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5B BINDING SITE, designated SEQ ID:45733, to the nucleotide sequence of VGAM50 RNA, herein designated VGAM RNA, also designated SEQ ID:2761.

[7188] A function of VGAM50 is therefore inhibition of Inositol Polyphosphate-5-phosphatase, 75kDa (INPP5B, Accession XM_170949), a gene which hydrolyzes the calcium-mobilizing second messenger $\text{ins}(1,4,5)\text{p3}$. Accordingly, utilities of VGAM50 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5B. The function of INPP5B has been established

by previous studies. The 75-kD inositol polyphosphate-5-phosphatase enzyme was originally isolated from human platelets and cloned from human megakaryocytic and placental cDNA libraries (Ross et al., 1991). It is 1 of at least 3 enzymes known to catalyze the conversion of inositol-1,4,5-triphosphate (IP3) to inositol-1,4-biphosphate (IP2). Three enzymes with this activity were identified: a 45-kD polypeptide, a 75-kD polypeptide, and a 120-kD polypeptide. By fluorescence in situ hybridization, Janne et al. (1994) found that the gene for the 75-kD enzyme (OMIM Ref. No. INPP5B) is located on band 1p34. The result was corroborated by Southern blot analysis of rodent/human hybrids containing portions of chromosome 1. Janne et al. (1995) determined that the mouse *Inpp5b* gene is located on distal mouse chromosome 4 within the conserved linkage group corresponding to human 1p. The gene is in the vicinity of the mouse developmental mutation 'dysgenetic lens' (*dyl*); however, using a genetic approach, Janne et al. (1995) showed that *Inpp5b* maps distal to *dyl* on mouse chromosome 4.

[7189] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7190] Janne, P. A.; Dutra, A. S.; Dracopoli, N. C.; Charnas, L. R.; Puck, J. M.; Nussbaum, R. L. : Localization of the 75-kDa inositol polyphosphate-5-phosphatase (INPP5B) to human chromosome band 1p34. Cytogenet. Cell Genet. 66: 164-166, 1994. ; and

[7191] Janne, P. A.; Rochelle, J. M.; Martin-DeLeon, P. A.; Stambolian, D.; Seldin, M. F.; Nussbaum, R. L. : Mapping of the 75-kDa inositol polyphosphate-5-phosphatase (Inpp5b) to distal mouse.

[7192] Further studies establishing the function and utilities of INPP5B are found in John Hopkins OMIM database record ID 147264, and in cited publications numbered 4973-4975 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 18 (KOX 11) (ZNF18, Accession XM_085596) is another VGAM50 host target gene. ZNF18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF18 BINDING SITE, designated SEQ ID:38249, to the nucleotide sequence of VGAM50 RNA, herein designated VGAM RNA,

also designated SEQ ID:2761.

[7193] Another function of VGAM50 is therefore inhibition of Zinc Finger Protein 18 (K0X 11) (ZNF18, Accession XM_085596). Accordingly, utilities of VGAM50 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF18. Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM_006549) is another VGAM50 host target gene. CAMKK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMKK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK2 BINDING SITE, designated SEQ ID:13310, to the nucleotide sequence of VGAM50 RNA, herein designated VGAM RNA, also designated SEQ ID:2761.

[7194] Another function of VGAM50 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM_006549). Accordingly, utilities of VGAM50 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK2. DKFZp547H025 (Accession NM_020161) is an-

other VGAM50 host target gene. DKFZp547H025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547H025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547H025 BINDING SITE, designated SEQ ID:21368, to the nucleotide sequence of VGAM50 RNA, herein designated VGAM RNA, also designated SEQ ID:2761.

[7195] Another function of VGAM50 is therefore inhibition of DKFZp547H025 (Accession NM_020161). Accordingly, utilities of VGAM50 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547H025. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 51 (VGAM51) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7196] VGAM51 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM51 was detected is described hereinabove with reference to Figs. 1–8.

[7197] VGAM51 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7198] VGAM51 gene encodes a VGAM51 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM51 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM51 precursor RNA is designated SEQ ID:37, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:37 is located at position 57805 relative to the genome of Invertebrate Iridescent Virus 6.

[7199] VGAM51 precursor RNA folds onto itself, forming VGAM51 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first

half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7200] An enzyme complex designated DICER COMPLEX, `dices` the VGAM51 folded precursor RNA into VGAM51 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM51 RNA is designated SEQ ID:2762, and is provided hereinbelow with reference to the sequence listing part.

[7201] VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM51 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7202] VGAM51 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM51 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM51 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM51 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7203] The complementary binding of VGAM51 RNA, herein designated VGAM RNA, to host target binding sites on VGAM51 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM51 host target RNA into VGAM51 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7204] It is appreciated that VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM51 host target genes. The mRNA of each one of this plurality of VGAM51 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM51 RNA, herein designated VGAM RNA, and which when bound by VGAM51 RNA causes inhibition of translation of respective one or more VGAM51 host target proteins.

[7205] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM51 gene, herein designated VGAM GENE, on one or more VGAM51 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7206] It is yet further appreciated that a function of VGAM51 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM51 correlate with, and may be deduced from, the identity of the host target genes which VGAM51 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7207] Nucleotide sequences of the VGAM51 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM51 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM51 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM51 are further described hereinbelow with reference to Table 1.

[7208] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM51 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM51 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7209] As mentioned hereinabove with reference to Fig. 1, a function of VGAM51 gene, herein designated VGAM is inhibition of expression of VGAM51 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM51 correlate with, and may be deduced from, the identity of the target genes which VGAM51 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7210] Desmin (DES, Accession XM_050962) is a VGAM51 host target gene. DES BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of DES BINDING SITE, designated SEQ ID:35692, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7211] A function of VGAM51 is therefore inhibition of Desmin (DES, Accession XM_050962). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DES. Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006) is another VGAM51 host target gene. FGF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF2 BINDING SITE, designated SEQ ID:7741, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7212] Another function of VGAM51 is therefore inhibition of Fibroblast Growth Factor 2 (basic) (FGF2, Accession NM_002006), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FGF2. The function of FGF2 has been established by previous studies. See fibroblast growth factor-12 (FGF12; 601513). By Southern blot hybridization of genomic DNA from rodent/human hybrid cell lines carrying individual human chromosomes, Smallwood et al. (1996) mapped the FHF2 gene (also symbolized FGF13) to the X chromosome. By using an interspecific backcross mapping panel, they demonstrated that the mouse gene, Fhf2, shows no recombination with the gene for CD40 antigen ligand (OMIM Ref. No. 300386). Thus the human gene is probably located at Xq26. By use of isotopic in situ hybridization, Lovec et al. (1997) assigned the FHF2 gene to Xq21. Gecz et al. (1999), however, provided evidence that the FHF2 gene is located in Xq26.3. They identified a male patient with features of Borjeson-Forssman-Lehmann syndrome (BFLS; 301900) and a duplication of the Xq26-q28 region. By FISH using YAC clones from Xq26, they localized the duplication breakpoint to an interval of approximately 400 kb in the Xq26.3 region between DXS155 and DXS294/DXS730. Database searches and an analysis of available genomic sequence from the region showed that the FHF2 gene is located within the duplication breakpoint

interval. Gecz et al. (1999) determined the structure of the FHF2 gene and identified 2 new exons, including a new 5-prime end exon, designated 1B. FHF2 is a large gene, extending over approximately 200 kb in Xq26.3, and contains at least 7 exons. It shows tissue-specific alternative splicing and alternative transcription starts. Northern blot hybridization showed highest expression in brain and skeletal muscle. The localization and tissue-specific expression pattern of FHF2 made it a possible candidate gene for familial cases of BFLS and for other syndromal and nonspecific forms of X-linked mental retardation mapping to that region. Animal model experiments lend further support to the function of FGF2.

[7213] It is appreciated that the abovementioned animal model for FGF2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7214] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7215] Gecz, J.; Baker, E.; Donnelly, A.; Ming, J. E.; McDonald-McGinn, D. M.; Spinner, N. B.; Zackai, E. H.; Sutherland, G. R.; Mulley, J. C. : Fibroblast growth factor homologous

factor 2 (FHF2): gene structure, expression and mapping to the Borjeson–Forssman–Lehmann syndrome region in Xq26 delineated by a duplication breakpoint in a BFLS–like patient. Hum. Genet. 104: 56–63, 1999. ; and

[7216] Lovec, H.; Hartung, H.; Verdier, A.–S.; Mattei, M.–G.; Birnbaum, D.; Goldfarb, M.; Coulier, F. : Assignment of FGF13 to human chromosome band Xq21 by in situ hybridization. Cytogenet.

[7217] Further studies establishing the function and utilities of FGF2 are found in John Hopkins OMIM database record ID 300070, and in cited publications numbered 9084–9086 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphodiesterase 4B, CAMP–specific (phosphodiesterase E4 duncce homolog, Drosophila) (PDE4B, Accession NM_002600) is another VGAM51 host target gene. PDE4B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDE4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4B BINDING SITE, designated SEQ ID:8467, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also desig–

nated SEQ ID:2762.

[7218] Another function of VGAM51 is therefore inhibition of Phosphodiesterase 4B, CAMP-specific (phosphodiesterase E4 dunce homolog, *Drosophila*) (PDE4B, Accession NM_002600), a gene which may be involved in mediating central nervous system effects of therapeutic agents ranging from antidepressants to antiasthmatic and anti-inflammatory agents. Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4B. The function of PDE4B has been established by previous studies. Huston et al. (1997) cloned a novel human (plus its cognate rat) PDE4B splice variant and compared its activities to the 2 other splice variants from this locus. Alternative splicing of mRNA generated from both the human and rat PDE4B genes produced long and short splice variants that had unique N-terminal regions. It was suggested that these alternatively spliced regions determined changes in the maximal catalytic activity of the isoforms, their susceptibility to inhibition by rolipram, and mode of interaction with particulate fractions. Milatovich et al. (1994) mapped the PDE4B gene to human 1p31 by a combination of Southern analysis of somatic cell hybrid lines and fluores-

cence in situ hybridization (FISH); they assigned the mouse homolog to chromosome 4 by Southern analysis of recombinant inbred (RI) mouse strains. Through the use of somatic cell hybrids segregating either human or rat chromosomes, Szpirer et al. (1995) mapped the PDE4B gene to human chromosome 1 and rat chromosome 5.

[7219] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7220] Huston, E.; Lumb, S.; Russell, A.; Catterall, C.; Ross, A. H.; Steele, M. R.; Bolger, G. B.; Perry, M. J.; Owens, R. J.; Houslay, M. D. : Molecular cloning and transient expression in COS7 cells of a novel human PDE4B cAMP-specific phosphodiesterase, HSPDE4B3. *Biochem. J.* 328: 549–558, 1997. ; and

[7221] Milatovich, A.; Bolger, G.; Michaeli, T.; Francke, U. : Chromosome localizations of genes for five cAMP-specific phosphodiesterases in man and mouse. *Somat. Cell Molec. Genet.* 20: 75–86.

[7222] Further studies establishing the function and utilities of PDE4B are found in John Hopkins OMIM database record ID 600127, and in cited publications numbered 1345, 1244 and 1346–1347 listed in the bibliography section

hereinbelow, which are also hereby incorporated by reference. Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM_012102) is another VGAM51 host target gene. RERE BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RERE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RERE BINDING SITE, designated SEQ ID:14407, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7223] Another function of VGAM51 is therefore inhibition of Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM_012102), a gene which binds DRPLA and locates in the nucleus. Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERE. The function of RERE has been established by previous studies. Northern blot analysis detected 2 RERE transcripts: one of 9 kb, expressed exclusively in pancreas and testis; and one of 7 kb, expressed most strongly in skeletal muscle with weaker expression in other tissues tested, including brain. The RERE protein migrated at an apparent molecular

weight of 212 kD in SDS-PAGE. An RERE fusion protein localized predominantly in the nucleus. Immunoprecipitation and in vitro binding assays demonstrated that the DRPLA and RERE proteins bind each other, which is facilitated by one of the RE repeats, and that extension of the DRPLA polyglutamine tract enhances the binding. Moreover, when RERE is overexpressed, the distribution of endogenous DRPLA protein alters from a diffuse to a speckled pattern in the nucleus so as to colocalize with RERE. More RERE protein is recruited into nuclear aggregates of the DRPLA protein with extended polyglutamine than into those of pure polyglutamine. The authors suggested a function for the DRPLA protein in the nucleus and the RE repeat in the protein-protein interaction. By study of a YAC spanning a translocation/duplication breakpoint within the minimally defined loss of heterozygosity region at 1p36.2-p36.1 in a neuroblastoma cell line, Amler et al. (2000) identified the RERE gene, which they designated DNB1/ARP (deleted in neuroblastoma-1/atrophin-related protein).

[7224] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [7225] Amler, L. C.; Bauer, A.; Corvi, R.; Dihlmann, S.; Praml, C.; Cavenee, W. K.; Schwab, M.; Hampton, G. M. : Identification and characterization of novel genes located at the t(1;15)(p36.2;q24) translocation breakpoint in the neuroblastoma cell line NGP. *Genomics* 64: 195–202, 2000. ; and
- [7226] Yanagisawa, H.; Bundo, M.; Miyashita, T.; Okamura-Oho, Y.; Tadokoro, K.; Tokunaga, K.; Yamada, M. : Protein binding of a DRPLA family through arginine–glutamic acid dipeptide repeats is.
- [7227] Further studies establishing the function and utilities of RERE are found in John Hopkins OMIM database record ID 605226, and in cited publications numbered 7304–7305 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ARG99 (Accession NM_031920) is another VGAM51 host target gene. ARG99 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARG99, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARG99 BINDING SITE, designated SEQ ID:25670, to the nucleotide sequence of VGAM51 RNA, herein designated

VGAM RNA, also designated SEQ ID:2762.

[7228] Another function of VGAM51 is therefore inhibition of ARG99 (Accession NM_031920). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARG99. FLJ12592 (Accession NM_032169) is another VGAM51 host target gene. FLJ12592 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12592, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12592 BINDING SITE, designated SEQ ID:25872, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7229] Another function of VGAM51 is therefore inhibition of FLJ12592 (Accession NM_032169). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12592. KIAA0266 (Accession NM_021645) is another VGAM51 host target gene. KIAA0266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0266, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0266 BINDING SITE, designated SEQ ID:22312, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7230] Another function of VGAM51 is therefore inhibition of KIAA0266 (Accession NM_021645). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0266. KIAA0478 (Accession NM_014870) is another VGAM51 host target gene. KIAA0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0478 BINDING SITE, designated SEQ ID:16979, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7231] Another function of VGAM51 is therefore inhibition of KIAA0478 (Accession NM_014870). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0478. KIAA0493 (Accession XM_034717) is another VGAM51 host target gene. KIAA0493 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0493 BINDING SITE, designated SEQ ID:32143, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7232] Another function of VGAM51 is therefore inhibition of KIAA0493 (Accession XM_034717). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0493. LOC127428 (Accession XM_059144) is another VGAM51 host target gene. LOC127428 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127428 BINDING SITE, designated SEQ ID:36900, to

the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7233] Another function of VGAM51 is therefore inhibition of LOC127428 (Accession XM_059144). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127428. LOC152313 (Accession XM_098190) is another VGAM51 host target gene. LOC152313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152313 BINDING SITE, designated SEQ ID:41470, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7234] Another function of VGAM51 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC201952 (Accession XM_117345) is another VGAM51 host target gene. LOC201952 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC201952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201952 BINDING SITE, designated SEQ ID:43397, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7235] Another function of VGAM51 is therefore inhibition of LOC201952 (Accession XM_117345). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201952. LOC220672 (Accession XM_017177) is another VGAM51 host target gene. LOC220672 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220672, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220672 BINDING SITE, designated SEQ ID:30308, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7236] Another function of VGAM51 is therefore inhibition of LOC220672 (Accession XM_017177). Accordingly, utilities

of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220672. LOC221395 (Accession XM_166354) is another VGAM51 host target gene. LOC221395 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221395 BINDING SITE, designated SEQ ID:44184, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7237] Another function of VGAM51 is therefore inhibition of LOC221395 (Accession XM_166354). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221395. LOC256529 (Accession XM_174314) is another VGAM51 host target gene. LOC256529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256529 BINDING SITE, designated SEQ ID:46588, to the nucleotide sequence of VGAM51 RNA, herein designated VGAM RNA, also designated SEQ ID:2762.

[7238] Another function of VGAM51 is therefore inhibition of LOC256529 (Accession XM_174314). Accordingly, utilities of VGAM51 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256529. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 52 (VGAM52) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7239] VGAM52 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM52 was detected is described hereinabove with reference to Figs. 1–8.

[7240] VGAM52 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7241] VGAM52 gene encodes a VGAM52 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM52 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM52 precursor RNA is designated SEQ ID:38, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:38 is located at position 109776 relative to the genome of Invertebrate Iridescent Virus 6.

[7242] VGAM52 precursor RNA folds onto itself, forming VGAM52 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7243] An enzyme complex designated DICER COMPLEX, `dices` the VGAM52 folded precursor RNA into VGAM52 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM52 RNA is designated SEQ ID:2763, and is provided hereinbelow with reference to the sequence listing part.

[7244] VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM52 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7245] VGAM52 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM52 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration,

Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM52 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7246] The complementary binding of VGAM52 RNA, herein designated VGAM RNA, to host target binding sites on VGAM52 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM52 host target RNA into VGAM52 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7247] It is appreciated that VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM52 host target genes. The mRNA of each one of this plurality of VGAM52 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM52 RNA, herein designated VGAM RNA, and which when bound by VGAM52 RNA causes inhibition of translation of respective one or more VGAM52 host target proteins.

[7248] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM52 gene, herein designated VGAM GENE, on one or more VGAM52 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective:

Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7249] It is yet further appreciated that a function of VGAM52 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM52 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM52 correlate with, and may be deduced from, the identity of the host target genes which VGAM52 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7250] Nucleotide sequences of the VGAM52 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM52 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM52 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM52 are further described hereinbelow with reference to Table 1.

[7251] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM52 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM52 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[7252] As mentioned hereinabove with reference to Fig. 1, a function of VGAM52 gene, herein designated VGAM is inhibition of expression of VGAM52 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM52 correlate with, and may be deduced from, the identity of the target genes which VGAM52 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7253] KIAA0205 (Accession NM_014873) is a VGAM52 host target gene. KIAA0205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0205 BINDING SITE, designated SEQ ID:17002, to the nucleotide sequence of VGAM52 RNA, herein designated VGAM RNA, also designated SEQ ID:2763.

[7254] A function of VGAM52 is therefore inhibition of KIAA0205 (Accession NM_014873). Accordingly, utilities of VGAM52 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with KIAA0205. Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815) is another VGAM52 host target gene. SLC5A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC5A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC5A7 BINDING SITE, designated SEQ ID:22389, to the nucleotide sequence of VGAM52 RNA, herein designated VGAM RNA, also designated SEQ ID:2763.

[7255] Another function of VGAM52 is therefore inhibition of Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815). Accordingly, utilities of VGAM52 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC5A7. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 53 (VGAM53) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7256] VGAM53 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM53 was detected is described hereinabove with reference to Figs. 1–8.

[7257] VGAM53 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7258] VGAM53 gene encodes a VGAM53 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM53 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM53 precursor RNA is designated SEQ ID:39, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:39 is located at position 157900 relative to the genome of Invertebrate Iridescent Virus 6.

[7259] VGAM53 precursor RNA folds onto itself, forming VGAM53 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin struc-

ture`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7260] An enzyme complex designated DICER COMPLEX, `dices` the VGAM53 folded precursor RNA into VGAM53 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM53 RNA is designated SEQ ID:2764, and is provided hereinbelow with reference to the sequence listing part.

[7261] VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM53 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING

and 3`UTR respectively.

[7262] VGAM53 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM53 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM53 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7263] The complementary binding of VGAM53 RNA, herein des-

ignated VGAM RNA, to host target binding sites on VGAM53 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM53 host target RNA into VGAM53 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7264] It is appreciated that VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM53 host target genes. The mRNA of each one of this plurality of VGAM53 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM53 RNA, herein designated VGAM RNA, and which when bound by VGAM53 RNA causes inhibition of translation of respective one or more VGAM53 host target proteins.

[7265] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM53 gene, herein designated VGAM GENE, on one or more VGAM53 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known

non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7266] It is yet further appreciated that a function of VGAM53 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM53 correlate with, and may be deduced from, the identity of the host target genes which VGAM53 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7267] Nucleotide sequences of the VGAM53 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM53 RNA, herein designated VGAM RNA, and

a schematic representation of the secondary folding of VGAM53 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM53 are further described hereinbelow with reference to Table 1.

[7268] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM53 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM53 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7269] As mentioned hereinabove with reference to Fig. 1, a function of VGAM53 gene, herein designated VGAM is inhibition of expression of VGAM53 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM53 correlate with, and may be deduced from, the identity of the target genes which VGAM53 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7270] Aconitase 1, Soluble (ACO1, Accession NM_002197) is a VGAM53 host target gene. ACO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACO1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACO1 BINDING SITE, designated SEQ ID:7954, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7271] A function of VGAM53 is therefore inhibition of Aconitase 1, Soluble (ACO1, Accession NM_002197), a gene which an iron-dependent enzyme; catalyzes conversion of citrate to cis-aconitate in the TCA cycle. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACO1. The function of ACO1 has been established by previous studies. Slaughter et al. (1975) reported that an electrophoretic survey had demonstrated 7 alleles at this locus. Among the populations studied, Nigerians showed polymorphism for ACON-S. Aconitase catalyzes the conversion of cis-aconitate to isocitrate. In studies of man-Chinese hamster somatic cell hybrids, Westerveld et al. (1975) showed that human gal-1-p uridyl transferase (GALT; 606999) and aconitase are syntenic. Eisenstein (2000) reviewed of the role of the iron regulatory proteins, IRP1 and IRP2 (OMIM Ref. No. 147582), and the molecular

control of mammalian iron metabolism. IRP1 is a bifunctional protein with mutually exclusive functions as an IRE RNA-binding protein or as the cytoplasmic isoform of aconitase. Aconitases are iron-sulfur proteins and a 4Fe-4S cluster is required for their enzymatic activity.

[7272] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7273] Slaughter, C. A.; Hopkinson, D. A.; Harris, H. : Aconitase polymorphism in man. *Ann. Hum. Genet.* 39: 193-202, 1975. ; and

[7274] Eisenstein, R. S. : Iron regulatory proteins and the molecular control of mammalian iron metabolism. *Annu. Rev. Nutr.* 20: 627-662, 2000.

[7275] Further studies establishing the function and utilities of ACO1 are found in John Hopkins OMIM database record ID 100880, and in cited publications numbered 181, 11582-183, 11882-805, 184, 806, 3401, 3780-186, 18 and 3864 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Attractin (ATRN, Accession NM_139321) is another VGAM53 host target gene. ATRN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by ATRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATRN BINDING SITE, designated SEQ ID:29300, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7276] Another function of VGAM53 is therefore inhibition of Attractin (ATRN, Accession NM_139321), a gene which is involved in the initial immune cell clustering during inflammatory response. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATRN. The function of ATRN has been established by previous studies. Attractin is a human serum glycoprotein that is rapidly expressed on activated T cells and released extracellularly after 48 to 72 hours. Duke-Cohan et al. (1998) cloned attractin and found that, as in its natural serum form, it mediates the spreading of monocytes that becomes the focus for the clustering of nonproliferating T lymphocytes. There are 2 mRNA species with hematopoietic tissue-specific expression that code for a 134-kD protein with a putative serine protease catalytic serine, 4 EGF-like motifs, a CUB do-

main, a C-type lectin domain, and a domain homologous with the ligand-binding region of the common gamma cytokine chain. Except for the last 2 domains, the overall structure shares high homology with a protein of *Caenorhabditis elegans*, suggesting that attractin has evolved new domains and functions in parallel with the development of cell-mediated immunity. When attractin was identified as the product of the murine 'mahogany' gene with connections to control of pigmentation and energy metabolism, and the 'mahogany' product was identified and shown to be a transmembrane protein, the possibility of a human membrane attractin in addition to the secreted form was raised. Tang et al. (2000) described the complete genomic sequence of attractin, focusing in particular on the exons coding for the 3-prime region, and showed how both human membrane and secreted attractin arise as a result of alternate splicing of the same gene. They found that soluble attractin arises from transcription of 25 sequential exons on 20p13, where the 3-prime terminal exon contains sequence from a long interspersed nuclear element-1 (OMIM Ref. No. LINE-1) retrotransposon insertion that includes a stop codon and a polyadenylation signal. The mRNA isoform for mem-

brane attraction splices over the LINE-1 exon and includes 5 exons encoding transmembrane and cytoplasmic domains with organization and coding potential almost identical to that of the mouse gene. The relative abundance of soluble and transmembrane isoforms measured by RT-PCR is differentially regulated in lymphoid tissues. Because activation of peripheral blood leukocytes with phytohemagglutinin induces strong expression of cell surface attractin followed by release of soluble attractin, these results suggested to Tang et al. (2000) that LINE-1 insertion, a genomic event unique to mammals, provided an evolutionarily mechanism for regulating cell interactions during an inflammatory reaction.

[7277] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7278] Duke-Cohan, J. S.; Gu, J.; McLaughlin, D. F.; Xu, Y.; Freeman, G. J.; Schlossman, S. F. : Attractin (DPPT-L), a member of the CUB family of cell adhesion and guidance proteins, is secreted by activated human T lymphocytes and modulates immune cell interactions. *Proc. Nat. Acad. Sci.* 95: 11336-11341, 1998. ; and

[7279] Tang, W.; Gunn, T. M.; McLaughlin, D. F.; Barsh, G. S.;

Schlossman, S. F.; Duke-Cohan, J. S. : Secreted and membrane attractin result from alternative splicing of the human ATRN gene. Pr.

[7280] Further studies establishing the function and utilities of ATRN are found in John Hopkins OMIM database record ID 603130, and in cited publications numbered 648-65 and 5172 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deltex Homolog 1 (Drosophila) (DTX1, Accession NM_004416) is another VGAM53 host target gene. DTX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DTX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DTX1 BINDING SITE, designated SEQ ID:10679, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7281] Another function of VGAM53 is therefore inhibition of Deltex Homolog 1 (Drosophila) (DTX1, Accession NM_004416), a gene which modulates Notch signalling and bHLH transcription factor activity. Accordingly, utilities of VGAM53 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DTX1. The function of DTX1 has been established by previous studies. Using the yeast interaction trap system, Matsuno et al. (1998) found that *Drosophila* and human deltex bind to the human SH3-domain containing protein GRB2 (OMIM Ref. No. 108355). Results from 2 different reporter assays allowed them for the first time to associate deltex with Notch-dependent transcriptional events. They presented evidence linking deltex to the modulation of basic helix-loop-helix (bHLH) transcription factor activity. After confirming that DTX1 is expressed in T lymphocytes at all stages of development, Izon et al. (2002) showed by RT-PCR analysis that murine Dtx1 is also expressed in hemopoietic stem cells and in B lymphocytes in all stages of development, whereas Notch1 expression is low in these cells. The authors transduced hemopoietic progenitor cells with Dtx1 expressing green fluorescent protein and found that mice with these cells had a marked decrease in T cells in the thymus, peripheral blood, and spleen. Instead, the thymus in these mice and in organ culture displayed B-cell development resembling the phenotype of mice deficient in Notch1. Expression of DTX1 partially inhibited transactivation of a CSL (RBPSUH;

147183)-dependent luciferase reporter by activated intracellular NOTCH1 (ICN1) in human and mouse cells. The N terminus of DTX1, which directly interacts with the NOTCH1 ankyrin repeats, inhibited transactivation by ICN1 possessing the ankyrin repeats, probably by inhibiting recruitment of coactivators to the C-terminal transactivation domain of NOTCH1. Izon et al. (2002) concluded that DTX1 is an inhibitor of NOTCH1 activity, a conclusion earlier suggested by the studies of Sestan et al. (1999) on dendritic outgrowth from human neurons.

[7282] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7283] Izon, D. J.; Aster, J. C.; He, Y.; Weng, A.; Karnell, F. G.; Patriub, V.; Xu, L.; Bakkour, S.; Rodriguez, C.; Allman, D.; Pear, W. S. : Deltex1 redirects lymphoid progenitors to the B cell lineage by antagonizing Notch1. *Immunity* 16: 231-243, 2002. ; and

[7284] Matsuno, K.; Eastman, D.; Mitsiades, T.; Quinn, A. M.; Cancianu, M. L.; Ordentlich, P.; Kadesch, T.; Artavanis-Tsakonas, S. : Human deltex is a conserved regulator of Notch signalling.

[7285] Further studies establishing the function and utilities of

DTX1 are found in John Hopkins OMIM database record ID 602582, and in cited publications numbered 5735, 9040-904 and 12352 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_012300) is another VGAM53 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:14664, SEQ ID:27366 and SEQ ID:27376 respectively, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7286] Another function of VGAM53 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_012300), a gene which somehow is involved in the process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25.GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491) is another VGAM53 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:27846 and SEQ ID:34445 respectively, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7287] Another function of VGAM53 is therefore inhibition of GRB2-associated Binding Protein 2 (GAB2, Accession NM_080491), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 has been established by previous studies. The GAB2

gene encodes a 100-kd adapter molecule that is the principal activator of phosphatidylinositol-3 kinase (PIK3; OMIM Ref. No. 171833) in response to activation of the high affinity IgE receptor (see OMIM Ref. No. 147140). Zhao et al. (1999) demonstrated that upon tyrosine phosphorylation, GAB2 physically interacts with SHP2 tyrosine phosphatase and GRB2 adapter protein (OMIM Ref. No. 604330). GAB2 has an inhibitory effect on the activation of ELK1 (OMIM Ref. No. 311040)-dependent transcription triggered by a dominant active Ras (OMIM Ref. No. 190020) mutant or under growth factor stimulation, whereas GAB1 acts to potentiate slightly the ELK1 activity in the same system. In contrast to the reciprocal effects of GAB1 and GAB2 in mediating ELK1 induction, these 2 molecules have a similar function in extracellular signal-regulated kinase activation induced by either oncogenic Ras or growth factor stimulation. Zhao et al. (1999) concluded that GAB1 and GAB2 may have distinct roles in coupling cytoplasmic-nuclear signal transduction. Animal model experiments lend further support to the function of GAB2. Gu et al. (2001) generated mice deficient in Gab2 by homologous recombination. Gab2 $-/-$ mice were viable and generally healthy; however, the response of Gab2 $-/-$

mast cells to stimulation of the high affinity IgE receptor Fc-epsilon-RI (see OMIM Ref. No. 147140) was defective. Accordingly, allergic reactions, such as passive cutaneous and systemic anaphylaxis, were markedly impaired in Gab^{-/-} mice. Biochemical analyses revealed that signaling pathways dependent on phosphatidylinositol-3 hydroxykinase (PI3K), a critical component of the Fc-epsilon-RI signaling, were defective in Gab2^{-/-} mast cells. Gu et al. (2001) concluded that GAB2 is the principal activator of PI3K in response to Fc-epsilon-RI activation, thereby providing genetic evidence that Dos/Gab family scaffolds regulate the PI3K pathway in vivo.

[7288] It is appreciated that the abovementioned animal model for GAB2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7289] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7290] Gu, H.; Saito, K.; Klamann, L. D.; Shen, J.; Fleming, T.; Wang, Y.-P.; Pratt, J. C.; Lin, G.; Lim, B.; Kinet, J.-P.; Neel, B. G. : Essential role for Gab2 in the allergic response. *Nature* 412: 186-190, 2001. ; and

- [7291] Zhao, C.; Yu, D.-H.; Shen, R.; Feng, G.-S. : Gab2, a new pleckstrin homology domain-containing adapter protein, acts to uncouple signaling from ERK kinase to Elk-1. J. Biol. Chem. 274.
- [7292] Further studies establishing the function and utilities of GAB2 are found in John Hopkins OMIM database record ID 606203, and in cited publications numbered 907, 673 and 7940 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SH3-domain Binding Protein 2 (SH3BP2, Accession NM_003023) is another VGAM53 host target gene. SH3BP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP2 BINDING SITE, designated SEQ ID:8949, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.
- [7293] Another function of VGAM53 is therefore inhibition of SH3-domain Binding Protein 2 (SH3BP2, Accession NM_003023). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with SH3BP2. SHC (Src homology 2 domain containing) Transforming Protein 1 (SHC1, Accession NM_003029) is another VGAM53 host target gene. SHC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHC1 BINDING SITE, designated SEQ ID:8971, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7294] Another function of VGAM53 is therefore inhibition of SHC (Src homology 2 domain containing) Transforming Protein 1 (SHC1, Accession NM_003029), a gene which couples activated growth factor receptors to a signaling pathway. Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHC1. The function of SHC1 has been established by previous studies. Nemoto and Finkel (2002) observed that exposure to intracellular reactive oxygen species (ROS) induced an increase in phosphorylated Fkhrl1 (OMIM Ref. No. 602681) and a shift from a nuclear to a cytosolic localization. They found that serum starva-

tion, a stimulus that increases oxidative stress, resulted in lower levels of hydrogen peroxide in Shc1 $-/-$ cells or in cells expressing a ser36-to-ala (S36A) Shc1 mutant compared with wildtype cells. Serum starvation also increased Fkhrl1-dependent transcriptional activity, which was further augmented in the Shc1-deficient cells. Increased ROS exposure failed to induce increased Fkhrl1 phosphorylation in the mutant cells. Promoter analysis of the catalase (CAT; 115500) gene established the presence of FKHRL1-binding sequences. Reporter assays showed FKHRL1 transactivates CAT, suggesting a capacity to augment antioxidant scavenging. Nemoto and Finkel (2002) concluded that there is an important functional relationship between forkhead proteins (e.g., FKHRL1), SHC1, and intracellular oxidants, all of which are thought to be involved in the aging process in worms and mammals. Animal model experiments lend further support to the function of SHC1. Using transgenic Cre-lox-p-mediated inducible expression of a phosphorylation-defective Shc mutant and, alternatively, conditional deletion of the Shc gene in mouse thymocytes, Zhang et al. (2002) showed that both expression and tyrosine phosphorylation of Shc have essential roles in thymic T-cell development. They

also provided a concise summary of SHC biology.

[7295] It is appreciated that the abovementioned animal model for SHC1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7296] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7297] Nemoto, S.; Finkel, T. : Redox regulation of forkhead proteins through a p66shc-dependent signaling pathway. Science 295: 2450–2452, 2002. ; and

[7298] Zhang, L.; Camerini, V.; Bender, T. P.; Ravichandran, K. S. : A nonredundant role for the adapter protein Shc in thymic T cell development. Nature Immun. 3: 749–755, 2002.

[7299] Further studies establishing the function and utilities of SHC1 are found in John Hopkins OMIM database record ID 600560, and in cited publications numbered 8158–8159, 50 and 8160–8165 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM_003056) is another VGAM53 host target gene. SLC19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by SLC19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A1 BINDING SITE, designated SEQ ID:9022, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7300] Another function of VGAM53 is therefore inhibition of Solute Carrier Family 19 (folate transporter), Member 1 (SLC19A1, Accession NM_003056). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A1. ABLIM (Accession NM_002313) is another VGAM53 host target gene. ABLIM BINDING SITE1 and ABLIM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABLIM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABLIM BINDING SITE1 and ABLIM BINDING SITE2, designated SEQ ID:8116 and SEQ ID:13549 respectively, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7301] Another function of VGAM53 is therefore inhibition of ABLIM (Accession NM_002313). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABLIM. BICD2 (Accession XM_046863) is another VGAM53 host target gene. BICD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BICD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BICD2 BINDING SITE, designated SEQ ID:34852, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7302] Another function of VGAM53 is therefore inhibition of BICD2 (Accession XM_046863). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BICD2. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769) is another VGAM53 host target gene. CHST4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHST4, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST4 BINDING SITE, designated SEQ ID:12337, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7303] Another function of VGAM53 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 4 (CHST4, Accession NM_005769). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST4. DKFZP434I0714 (Accession XM_098247) is another VGAM53 host target gene. DKFZP434I0714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434I0714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I0714 BINDING SITE, designated SEQ ID:41530, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7304] Another function of VGAM53 is therefore inhibition of DKFZP434I0714 (Accession XM_098247). Accordingly, utili-

ties of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I0714. Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969) is another VGAM53 host target gene. EIF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5 BINDING SITE, designated SEQ ID:7701, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7305] Another function of VGAM53 is therefore inhibition of Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5. FLJ00001 (Accession XM_088525) is another VGAM53 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FLJ00001 BINDING SITE, designated SEQ ID:39783, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7306] Another function of VGAM53 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ10101 (Accession NM_024718) is another VGAM53 host target gene. FLJ10101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10101 BINDING SITE, designated SEQ ID:24048, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7307] Another function of VGAM53 is therefore inhibition of FLJ10101 (Accession NM_024718). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10101. FLJ10209 (Accession NM_018026) is another VGAM53

host target gene. FLJ10209 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10209 BINDING SITE, designated SEQ ID:19769, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7308] Another function of VGAM53 is therefore inhibition of FLJ10209 (Accession NM_018026). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10209. FLJ20344 (Accession NM_017776) is another VGAM53 host target gene. FLJ20344 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20344, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20344 BINDING SITE, designated SEQ ID:19404, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7309] Another function of VGAM53 is therefore inhibition of FLJ20344 (Accession NM_017776). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20344. G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_057169) is another VGAM53 host target gene. GIT2 BINDING SITE1 through GIT2 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GIT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE1 through GIT2 BINDING SITE3, designated SEQ ID:27687, SEQ ID:27700 and SEQ ID:16605 respectively, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7310] Another function of VGAM53 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_057169). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. KIAA0174 (Accession XM_085981) is another VGAM53 host target gene. KIAA0174 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by KIAA0174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0174 BINDING SITE, designated SEQ ID:38432, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7311] Another function of VGAM53 is therefore inhibition of KIAA0174 (Accession XM_085981). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0174. KIAA0562 (Accession NM_014704) is another VGAM53 host target gene. KIAA0562 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0562 BINDING SITE, designated SEQ ID:16243, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7312] Another function of VGAM53 is therefore inhibition of

KIAA0562 (Accession NM_014704). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0562. KIAA0652 (Accession NM_014741) is another VGAM53 host target gene. KIAA0652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0652 BINDING SITE, designated SEQ ID:16409, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7313] Another function of VGAM53 is therefore inhibition of KIAA0652 (Accession NM_014741). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0652. KIAA0876 (Accession XM_035625) is another VGAM53 host target gene. KIAA0876 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0876 BINDING SITE, designated SEQ ID:32299, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7314] Another function of VGAM53 is therefore inhibition of KIAA0876 (Accession XM_035625). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0876. KIAA0960 (Accession XM_166543) is another VGAM53 host target gene. KIAA0960 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0960 BINDING SITE, designated SEQ ID:44520, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7315] Another function of VGAM53 is therefore inhibition of KIAA0960 (Accession XM_166543). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0960. KIAA1303 (Accession XM_038376) is another

VGAM53 host target gene. KIAA1303 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1303 BINDING SITE, designated SEQ ID:32834, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7316] Another function of VGAM53 is therefore inhibition of KIAA1303 (Accession XM_038376). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1303. KIAA1423 (Accession XM_029703) is another VGAM53 host target gene. KIAA1423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1423 BINDING SITE, designated SEQ ID:30920, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7317] Another function of VGAM53 is therefore inhibition of KIAA1423 (Accession XM_029703). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1423. KIAA1701 (Accession XM_042087) is another VGAM53 host target gene. KIAA1701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1701 BINDING SITE, designated SEQ ID:33685, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7318] Another function of VGAM53 is therefore inhibition of KIAA1701 (Accession XM_042087). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1701. MGC16179 (Accession NM_032766) is another VGAM53 host target gene. MGC16179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16179, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16179 BINDING SITE, designated SEQ ID:26514, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7319] Another function of VGAM53 is therefore inhibition of MGC16179 (Accession NM_032766). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16179. MKP-7 (Accession XM_039106) is another VGAM53 host target gene. MKP-7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKP-7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKP-7 BINDING SITE, designated SEQ ID:33008, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7320] Another function of VGAM53 is therefore inhibition of MKP-7 (Accession XM_039106). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKP-7.

PRO1770 (Accession NM_014100) is another VGAM53 host target gene. PRO1770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1770, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1770 BINDING SITE, designated SEQ ID:15326, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7321] Another function of VGAM53 is therefore inhibition of PRO1770 (Accession NM_014100). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1770. Rab11-FIP2 (Accession NM_014904) is another VGAM53 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17097, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA,

also designated SEQ ID:2764.

[7322] Another function of VGAM53 is therefore inhibition of Rab11-FIP2 (Accession NM_014904). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rab11-FIP2. UBX Domain Containing 2 (UBXD2, Accession XM_043196) is another VGAM53 host target gene. UBXD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBXD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBXD2 BINDING SITE, designated SEQ ID:33913, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7323] Another function of VGAM53 is therefore inhibition of UBX Domain Containing 2 (UBXD2, Accession XM_043196). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBXD2. LOC147054 (Accession XM_097172) is another VGAM53 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40792, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7324] Another function of VGAM53 is therefore inhibition of LOC147054 (Accession XM_097172). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC154881 (Accession XM_088063) is another VGAM53 host target gene. LOC154881 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154881, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154881 BINDING SITE, designated SEQ ID:39497, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7325] Another function of VGAM53 is therefore inhibition of LOC154881 (Accession XM_088063). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC154881. LOC157858 (Accession XM_098833) is another VGAM53 host target gene. LOC157858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157858 BINDING SITE, designated SEQ ID:41867, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7326] Another function of VGAM53 is therefore inhibition of LOC157858 (Accession XM_098833). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157858. LOC196047 (Accession XM_116883) is another VGAM53 host target gene. LOC196047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196047 BINDING SITE, designated SEQ ID:43146, to

the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7327] Another function of VGAM53 is therefore inhibition of LOC196047 (Accession XM_116883). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196047. LOC253286 (Accession XM_174256) is another VGAM53 host target gene. LOC253286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253286 BINDING SITE, designated SEQ ID:46585, to the nucleotide sequence of VGAM53 RNA, herein designated VGAM RNA, also designated SEQ ID:2764.

[7328] Another function of VGAM53 is therefore inhibition of LOC253286 (Accession XM_174256). Accordingly, utilities of VGAM53 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253286. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 54 (VGAM54) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7329] VGAM54 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM54 was detected is described hereinabove with reference to Figs. 1–8.

[7330] VGAM54 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7331] VGAM54 gene encodes a VGAM54 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM54 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM54 precursor RNA is designated SEQ ID:40, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:40 is located at position 169568 relative to the genome of Invertebrate Iridescent Virus 6.

[7332] VGAM54 precursor RNA folds onto itself, forming VGAM54 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7333] An enzyme complex designated DICER COMPLEX, `dices` the VGAM54 folded precursor RNA into VGAM54 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM54 RNA is designated SEQ ID:2765, and is provided hereinbelow with reference to the sequence listing part.

[7334] VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM54 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM54 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7335] VGAM54 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM54 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM54 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region,

this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7336] The complementary binding of VGAM54 RNA, herein designated VGAM RNA, to host target binding sites on VGAM54 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM54 host target RNA into VGAM54 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7337] It is appreciated that VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM54 host target genes. The mRNA of each one of this plurality of VGAM54 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM54 RNA, herein designated VGAM RNA, and which when bound by VGAM54 RNA causes inhibition of translation of respective one or more VGAM54 host target proteins.

[7338] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM54 gene, herein designated VGAM GENE, on one or more VGAM54 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7339] It is yet further appreciated that a function of VGAM54 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM54 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM54 correlate with, and may be deduced from, the identity of the host target genes which VGAM54 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7340] Nucleotide sequences of the VGAM54 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM54 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM54 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM54 are further described hereinbelow with reference to Table 1.

[7341] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM54 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM54 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7342] As mentioned hereinabove with reference to Fig. 1, a function of VGAM54 gene, herein designated VGAM is inhibition of expression of VGAM54 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM54 correlate with, and may be deduced from, the identity of the target genes which VGAM54 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7343] Proline-rich Gla (G-carboxyglutamic acid) Polypeptide 1 (PRRG1, Accession NM_000950) is a VGAM54 host target gene. PRRG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRRG1 BINDING SITE, designated SEQ ID:6653, to the nucleotide sequence of VGAM54 RNA, herein designated VGAM RNA, also designated SEQ ID:2765.

[7344] A function of VGAM54 is therefore inhibition of Proline-rich Gla (G-carboxyglutamic acid) Polypeptide 1 (PRRG1, Accession NM_000950). Accordingly, utilities of VGAM54 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRRG1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 55 (VGAM55) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7345] VGAM55 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM55 was detected is described hereinabove with reference to Figs. 1–8.

[7346] VGAM55 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7347] VGAM55 gene encodes a VGAM55 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM55 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM55 precursor RNA is designated SEQ ID:41, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:41 is located at position 37014 relative to the genome of Invertebrate Iridescent Virus 6.

[7348] VGAM55 precursor RNA folds onto itself, forming VGAM55 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is

due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7349] An enzyme complex designated DICER COMPLEX, `dices` the VGAM55 folded precursor RNA into VGAM55 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM55 RNA is designated SEQ ID:2766, and is provided hereinbelow with reference to the sequence listing part.

[7350] VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM55 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7351] VGAM55 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM55 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM55 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7352] The complementary binding of VGAM55 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM55 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM55 host target RNA into VGAM55 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7353] It is appreciated that VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM55 host target genes. The mRNA of each one of this plurality of VGAM55 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM55 RNA, herein designated VGAM RNA, and which when bound by VGAM55 RNA causes inhibition of translation of respective one or more VGAM55 host target proteins.

[7354] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM55 gene, herein designated VGAM GENE, on one or more VGAM55 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7355] It is yet further appreciated that a function of VGAM55 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM55 correlate with, and may be deduced from, the identity of the host target genes which VGAM55 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7356] Nucleotide sequences of the VGAM55 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM55 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM55 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM55 are further described hereinbelow with reference to Table 1.

[7357] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM55 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM55 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7358] As mentioned hereinabove with reference to Fig. 1, a function of VGAM55 gene, herein designated VGAM is inhibition of expression of VGAM55 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM55 correlate with, and may be deduced from, the identity of the target genes which VGAM55 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7359] Aristaless-like Homeobox 3 (ALX3, Accession NM_006492) is a VGAM55 host target gene. ALX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALX3, corresponding to a HOST TARGET binding site such as BINDING SITE

I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALX3 BINDING SITE, designated SEQ ID:13221, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7360] A function of VGAM55 is therefore inhibition of Arista-less-like Homeobox 3 (ALX3, Accession NM_006492), a gene which is involved in cell-type differentiation and development. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALX3. The function of ALX3 has been established by previous studies. Homeo box genes encode transcriptional regulators involved in cell-type differentiation and development. To identify beta-cell homeodomain proteins, Rudnick et al. (1994) designed primers based on the sequences of the beta-cell homeo box genes cdx3 (OMIM Ref. No. 600297), Imx1 (OMIM Ref. No. 600298), and the Drosophila homeodomain protein Antennapedia to amplify inserts by PCR from a hamster insulinoma cDNA library (HIT). One of the genes identified showed homology to the Drosophila gene aristaless and was designated Alx3. Alx3 encodes a paired (prd) class homeodomain protein that shares high sequence homol-

ogy with another member of this subclass, *cart1* (OMIM Ref. No. 601527), not only in the homeodomain but also in the region between the homeodomain and the C terminus. In addition to HIT cells, *Alx3* was expressed in a mouse pancreatic exocrine cell line and was abundant in pancreatic exocrine cells. Ten Berge et al. (1998) cloned a full-length mouse *Alx3* cDNA encoding a 343-amino acid protein. *Alx3* belongs to the large class of genes that encode a prd/Q50 homeodomain, denoting moderate similarity to the prd homeodomain but the presence of a glutamine at position 50. The authors found that *Alx3* was expressed in mouse embryos from 8 days of gestation onward in a characteristic pattern, predominantly in neural crest-derived mesenchyme and in lateral plate mesoderm. Prominent expression was seen in the frontonasal head mesenchyme and in the first and second pharyngeal arches and some of their derivatives. High expression was also seen in the tail and in many derivatives of the lateral plate mesoderm including the limbs, the body wall, and the genital tubercle. By interspecific backcross analysis, ten Berge et al. (1998) mapped the mouse *Alx3* gene to chromosome 3 in close proximity to the droopy-ear mutation (*de*). The International Radiation Hybrid Mapping

Consortium mapped the human ALX3 gene to chromosome 1p21-p13 (stSG24507

[7361] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7362] Rudnick, A.; Ling, T. Y.; Odagiri, H.; Rutter, W. J.; German, M. S. : Pancreatic beta cells express a diverse set of homeobox genes. Proc. Nat. Acad. Sci. 91: 12203-12207, 1994. ; and

[7363] ten Berge, D.; Brouwer, A.; El Bahi, S.; Guenet, J.-L.; Robert, B.; Meijlink, F. : Mouse Alx3: an aristaless-like homeobox gene expressed during embryogenesis in ectomesenchyme and late.

[7364] Further studies establishing the function and utilities of ALX3 are found in John Hopkins OMIM database record ID 606014, and in cited publications numbered 6336-6337 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM_001174) is another VGAM55 host target gene. ARHGAP6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP6 BINDING SITE, designated SEQ ID:6848, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7365] Another function of VGAM55 is therefore inhibition of Rho GTPase Activating Protein 6 (ARHGAP6, Accession NM_001174), a gene which activates the rho-type GTPases by converting them to an inactive GTP-bound state. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP6. The function of ARHGAP6 has been established by previous studies. In a search for the genetic defect in microphthalmia with linear skin defects syndrome (MLS; 309801), Schaefer et al. (1997) trapped exons from 14 overlapping cosmids from the 500-kb MLS critical region in Xp22.3. Using exon connection followed by cDNA library screening, they identified a 2.4-kb contig of cDNA clones spanning 170 kb of genomic sequence in the MLS deletion region. Northern analysis of this cDNA detected a prominent transcript of approximately 4.2 kb and a less abundant transcript of approximately 6 kb in all tissues examined, with additional transcripts in skeletal

muscle. Sequence analysis revealed a coding region of 601 amino acids contained in 12 exons, with a splice variant isoform of 495 amino acids. The predicted protein sequence of the gene, symbolized ARHGAP6, contains homology to the GTPase-activating (GAP) domain of the Rho-GAP family of proteins (e.g., 300023), which has been implicated in the regulation of actin polymerization at the plasma membrane in several cellular processes. Schaefer et al. (1997) discussed reasons for thinking that a defect in the Rho pathway may play a role in the pathogenesis of MLS syndrome. Prakash et al. (2000) investigated the function of ARHGAP6 by generating Arhgap6 null mice and also by in vitro expression studies. Surprisingly, loss of the rhoGAP function of Arhgap6 did not cause any detectable phenotypic or behavioral abnormalities in the mutant mice. Transfected mammalian cells expressing ARHGAP6 lost their actin stress fibers, retracted from the growth surface, and extended thin, branching processes resembling filopodia. The ARHGAP6 protein colocalized with actin filaments through an N-terminal domain and recruited filamentous actin into the growing processes. Mutation of a conserved arginine residue in the rhoGAP domain prevented the loss of stress fibers but had

little effect on process outgrowth. The authors concluded that ARHGAP6 has 2 independent functions: one as a GAP with specificity for RhoA and the other as a cytoskeletal protein that promotes actin remodeling.

[7366] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7367] Prakash, S. K.; Paylor, R.; Jenna, S.; Lamarche-Vane, N.; Armstrong, D. L.; Xu, B.; Mancini, M. A.; Zoghbi, H. Y. : Functional analysis of ARHGAP6, a novel GTPase-activating protein for RhoA. Hum. Molec. Genet. 9: 477-488, 2000. ; and

[7368] Schaefer, L.; Prakash, S.; Zoghbi, H. Y. : Cloning and characterization of a novel rho-type GTPase-activating protein gene (ARHGAP6) from the critical region for microphthalmia with li.

[7369] Further studies establishing the function and utilities of ARHGAP6 are found in John Hopkins OMIM database record ID 300118, and in cited publications numbered 10628-10629 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM_042963) is another

VGAM55 host target gene. ARHGEF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF6 BINDING SITE, designated SEQ ID:33842, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7370] Another function of VGAM55 is therefore inhibition of Rac/Cdc42 Guanine Nucleotide Exchange Factor (GEF) 6 (ARHGEF6, Accession XM_042963). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF6. Activating Transcription Factor 7 (ATF7, Accession NM_006856) is another VGAM55 host target gene. ATF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF7 BINDING SITE, designated SEQ ID:13726, to the nucleotide sequence of VGAM55 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2766.

[7371] Another function of VGAM55 is therefore inhibition of Activating Transcription Factor 7 (ATF7, Accession NM_006856). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF7. HLA-B Associated Transcript 1 (BAT1, Accession NM_004640) is another VGAM55 host target gene. BAT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAT1 BINDING SITE, designated SEQ ID:11015, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7372] Another function of VGAM55 is therefore inhibition of HLA-B Associated Transcript 1 (BAT1, Accession NM_004640), a gene which associates with the major histocompatibility complex, a negative regulator of inflammation. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAT1. The function of BAT1 has

been established by previous studies. Peelman et al. (1995) sequenced both human and pig BAT1 and showed that the genes are members of the DEAD-box family of ATP-dependent RNA helicases, members of which are involved in a number of cellular functions including initiation of translation, RNA splicing, and ribosome assembly. Proteins of this family have 9 conserved amino acid motifs but differ at their amino and carboxyl ends. From studies of other family members, the first block is involved in ATP binding, the fifth block may be an ATPase, the sixth block is needed for RNA helicase activity, and the ninth block is involved with ATP hydrolysis-independent RNA interactions during unwinding. The gene contains 10 exons spanning about 10 kb of genomic DNA and encodes a 428-amino acid protein. Peelman et al. (1995) detected 3 different length mRNAs (4.1, 17, and 0.9 kb) in all tissues analyzed, although at different relative levels. The protein is highly conserved, with 98% identity to the p47 rat liver nuclear protein and 99% identity to the pig BAT1 homolog. Furthermore, the location of BAT1 at the telomeric end of the class III region is conserved in both humans and pig. Peelman et al. (1995) showed that a recombinant epitope-tagged BAT1 construct was expressed in COS cells and

showed localization of the protein to the nucleus. Allcock et al. (2001) used antisense DNA corresponding to exons 2 through 5 of the BAT1 gene and showed that after antigenic stimulation, monocytic and T-cell lines produced higher levels of the acute phase cytokines TNF, interleukin-1 (IL1; OMIM Ref. No. 147760), and IL6 (OMIM Ref. No. 147620) than cells containing the transfecting vector alone. These results suggested that BAT1 is a negative regulator of inflammation.

[7373] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7374] Peelman, L. J.; Chardon, P.; Nunes, M.; Renard, C.; Gefrotin, C.; Vaiman, M.; Van Zeveren, A.; Coppieters, W.; van de Weghe, A.; Bouquet, Y.; Choy, W. W.; Strominger, J. L.; Spies, T. : The BAT1 gene in the MHC encodes an evolutionarily conserved putative nuclear RNA helicase of the DEAD family. *Genomics* 26: 210–218, 1995. ; and

[7375] Allcock, R. J. N.; Williams, J. H.; Price, P. : The central MHC gene, BAT1, may encode a protein that down-regulates cytokine production. *Genes Cells* 6: 487–494, 2001.

[7376] Further studies establishing the function and utilities of BAT1 are found in John Hopkins OMIM database record ID

142560, and in cited publications numbered 3541–3545 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CD34 Antigen (CD34, Accession NM_001773) is another VGAM55 host target gene. CD34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD34 BINDING SITE, designated SEQ ID:7532, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7377] Another function of VGAM55 is therefore inhibition of CD34 Antigen (CD34, Accession NM_001773), a gene which is a monomeric cell surface antigen that is selectively expressed on human hematopoietic progenitor cells. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD34. The function of CD34 has been established by previous studies. CD34 is a monomeric cell surface antigen with a molecular mass of approximately 110 kD that is selectively expressed on human

hematopoietic progenitor cells. In the hands of Sutherland et al. (1988), partial amino acid analysis of highly purified CD34 antigen revealed no significant sequence similarity with any previously described structures. Sequential immunoprecipitation and Western blot analysis indicated that this antigen is not a member of the leukosialin/sialophorin family, despite the fact that these molecules share several structural similarities. Animal model experiments lend further support to the function of CD34. To analyze the involvement of CD34 in hematopoiesis, Cheng et al. (1996) produced both embryonic stem (ES) cells in mice null for the expression of this mucin. Analysis of yolk sac-like hematopoietic development in embryoid bodies derived from CD34-null ES cells showed a significant delay in both erythroid and myeloid differentiation that could be reversed by transfection of the mutant ES cells with CD34 constructs expressing either a complete or truncated cytoplasmic domain. In spite of these diminished embryonic hematopoietic progenitor numbers, the CD34-null mice developed normally, and the hematopoietic profile of adult blood appeared typical. However, the colony-forming activity of hematopoietic progenitors derived from both bone marrow and spleen was significantly

reduced in adult CD34-deficient animals.

[7378] It is appreciated that the abovementioned animal model for CD34 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7379] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7380] Cheng, J.; Baumhueter, S.; Cacalano, G.; Carver-Moore, K.; Thibodeaux, H.; Thomas, R.; Broxmeyer, H. E.; Cooper, S.; Hague, N.; Moore, M.; Lasky, L. A. : Hematopoietic defects in mice lacking the sialomucin CD34. Blood 87: 479-490, 1996. ; and

[7381] Sutherland, D. R.; Watt, S. M.; Dowden, G.; Karhi, K.; Baker, M. A.; Greaves, M. F.; Smart, J. E. : Structural and partial amino acid sequence analysis of the human hemopoietic progenitor.

[7382] Further studies establishing the function and utilities of CD34 are found in John Hopkins OMIM database record ID 142230, and in cited publications numbered 2673-2681 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2,

Accession NM_006482) is another VGAM55 host target gene. DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK2 BINDING SITE1 and DYRK2 BINDING SITE2, designated SEQ ID:13210 and SEQ ID:9635 respectively, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7383] Another function of VGAM55 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 2 (DYRK2, Accession NM_006482). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK2. Forkhead Box E1 (thyroid transcription factor 2) (FOXE1, Accession NM_004473) is another VGAM55 host target gene. FOXE1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FOXE1 BINDING SITE, designated SEQ ID:10785, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7384] Another function of VGAM55 is therefore inhibition of Forkhead Box E1 (thyroid transcription factor 2) (FOXE1, Accession NM_004473). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXE1. Glutamate Receptor, Ionotropic, N-methyl D-aspartate-like 1A (GRINL1A, Accession XM_045376) is another VGAM55 host target gene. GRINL1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRINL1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRINL1A BINDING SITE, designated SEQ ID:34446, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7385] Another function of VGAM55 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate-like 1A (GRINL1A, Accession XM_045376), a gene

which plays a role in the development and function of the mammalian brain. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRINL1A. The function of GRINL1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943) is another VGAM55 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38416, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7386] Another function of VGAM55 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with GRLF1. The function of GRLF1 has been established by previous studies. Using polyclonal antibodies against purified GRLF1, LeClerc et al. (1991) isolated a partial GRLF1 cDNA encoding a deduced 835-amino acid protein. The protein contains 3 possible zinc finger structures and a leucine zipper motif that contains 1 cysteine. Western blot analysis detected expression of a 94-kD GRLF1 protein. By sequence comparisons with rat p190A, database searching, and RT-PCR analysis, Tikoo et al. (2000) obtained a full-length cDNA sequence encoding GRLF1, the human homolog of p190A. The deduced 1,514-amino acid protein is 97% identical to the rat sequence. The first 1,287 residues, including the GTPase and middle domains, are encoded by the 3.7-kb exon 1, similar to the structure observed in p190B (ARHGAP5; 602680).

[7387] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7388] LeClerc, S.; Palaniswami, R.; Xie, B.; Govdan, M. V. : Molecular cloning and characterization of a factor that binds the human glucocorticoid receptor gene and represses its expression. J. Biol. Chem. 266: 17333-17340, 1991. ; and

- [7389] Tikoo, A.; Czekay, S.; Viars, C.; White, S.; Heath, J. K.; Arden, K.; Maruta, H. : p190-A, a human tumor suppressor gene, maps to the chromosomal region 19q13.3 that is reportedly delet.
- [7390] Further studies establishing the function and utilities of GRLF1 are found in John Hopkins OMIM database record ID 605277, and in cited publications numbered 6613–6614 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lipoprotein Lipase (LPL, Accession NM_000237) is another VGAM55 host target gene. LPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPL BINDING SITE, designated SEQ ID:5752, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.
- [7391] Another function of VGAM55 is therefore inhibition of Lipoprotein Lipase (LPL, Accession NM_000237), a gene which is the hydrolysis of triglycerides of circulating chylomicrons and very low density lipoproteins (vldl). the en-

zyme functions in the presence of apolipoprotein c-2 on the luminal surface of vascular. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPL. The function of LPL has been established by previous studies. Holt et al. (1939) first reported the familial occurrence of this syndrome. Boggs et al. (1957) described 3 affected sibs from a first-cousin mating. Massive hyperchylomicronemia occurs when the patient is on a normal diet and disappears completely in a few days on fat-free feeding. On a normal diet alpha and beta lipoproteins are low. A defect in removal of chylomicrons (fat induction) and of other triglyceride-rich lipoproteins (carbohydrate induction) is present. Decreased plasma postheparin lipolytic activity (PHLA) is demonstrated. Low tissue activity of lipoprotein lipase was suspected. The full-blown disease, manifested by attacks of abdominal pain, hepatosplenomegaly, eruptive xanthomas, and lactescence of the plasma, is a recessive. Heterozygotes may show slight hyperlipemia and reduced PHLA. Precocious atherosclerosis does not seem to be a feature. Havel and Gordon (1960) first recognized deficiency of lipoprotein lipase (triacylglycerol acylhydrolase; EC 3.1.1.3) as the basic de-

fect in type I hyperlipoproteinemia. The type I hyperlipoproteinemia phenotype can also result from deficiency of the activator of lipoprotein lipase, apolipoprotein C-II (Breckenridge et al., 1978)--see 207750. This condition was called fat-induced hypertriglyceridemia by Nevin and Slack (1968). Adipose tissue in heterozygotes shows intermediate levels of lipoprotein lipase. Berger (1987) reported a case of variant lipoprotein lipase deficiency in which muscle lipoprotein lipase was essentially normal although the enzyme in adipose tissue was markedly reduced. Schreibman et al. (1973) studied a family with 2 clinically typical sibs whose lipoprotein lipase showed abnormal substrate specificity and kinetics. Hoeg et al. (1983) reported an extraordinary patient in whom the diagnosis was first made at the age of 75. Absolute abstinence from alcohol and a self-imposed low-fat diet may have been responsible for the long survival. Since childhood, he had had recurrent abdominal pain, nausea and vomiting, diagnosed as 'gall bladder attacks,' until age 48 when he was first hospitalized. During the next 15 years he had 1 to 3 episodes of abdominal pain per year necessitating hospitalization. These episodes were diagnosed as acute pancreatitis and were sometimes associated with

an evanescent papular rash. Jaundice that developed rapidly at age 64 was found to be due to bile duct stenosis, which was surgically relieved. He had, at age 73, ischemic heart disease and a femoral bruit. Animal model experiments lend further support to the function of LPL. To study the effects of increased free fatty acid (FFA) uptake in muscle tissue, Levak-Frank et al. (1995) generated transgenic mice carrying a human LPL minigene driven by the promoter of the muscle creatine kinase gene (OMIM Ref. No. 123310). In these mice, human LPL was expressed in skeletal muscle and cardiac muscle, but not in other tissues. In 3 independent transgenic mouse lines, the authors detected decreased plasma triglyceride levels, elevated FFA uptake by muscle tissue, weight loss, and premature death in proportion to the level of LPL overexpression. The animals developed severe myopathy characterized by muscle fiber degeneration, fiber atrophy, glycogen storage, and extensive proliferation of mitochondria and peroxisomes. The extensive proliferation suggested to Levak-Frank et al. (1995) that FFA plays an important role in the biogenesis of these organelles. The experiments indicated that LPL is rate-limiting for the supply of muscle tissue with triglyceride-derived FFA. The

authors concluded that improper regulation of muscle LPL can lead to major pathologic changes and may be important in the pathogenesis of some human myopathies

[7392] It is appreciated that the abovementioned animal model for LPL is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7393] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7394] Berger, G. M. B. : An incomplete form of familial lipoprotein lipase deficiency presenting with type I hyperlipoproteinemia. *Am. J. Clin. Path.* 88: 369–373, 1987. ; and

[7395] Levak–Frank, S.; Radner, H.; Walsh, A.; Stollberger, R.; Knipping, G.; Hoefler, G.; Sattler, W.; Weinstock, P. H.; Breslow, J. L.; Zechner, R. : Muscle–specific overexpression of lipoprot.

[7396] Further studies establishing the function and utilities of LPL are found in John Hopkins OMIM database record ID 238600, and in cited publications numbered 3301–3304, 3473–3320, 1866, 11733–11735, 11661, 11736–11741, 3300, 11742–11757, 3321–3323, 4211, 8952–8954, 8958–8956, 8959, 8960–8969, 9234–8971, 9236–8974,

9235, 9408, 9416–9419, 11382–943 and 36 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Melanoma Antigen, Family B, 4 (MAGEB4, Accession NM_002367) is another VGAM55 host target gene. MAGEB4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAGEB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAGEB4 BINDING SITE, designated SEQ ID:8175, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7397] Another function of VGAM55 is therefore inhibition of Melanoma Antigen, Family B, 4 (MAGEB4, Accession NM_002367). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAGEB4. Mitogen-activated Protein Kinase Kinase Kinase 14 (MAP3K14, Accession NM_003954) is another VGAM55 host target gene. MAP3K14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K14, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K14 BINDING SITE, designated SEQ ID:10090, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7398] Another function of VGAM55 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 14 (MAP3K14, Accession NM_003954), a gene which is involved in the activation of nf-kappa-b and its transcriptional activity. induces the processing of nf-kappa-b 2/p100. could act in a receptor-selective manner (by similarity). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K14. The function of MAP3K14 has been established by previous studies. By functional analysis of NIK and a kinase-deficient NIK expressed in primary human cells and in inflamed rheumatoid arthritis tissue, Smith et al. (2001) showed that NIK has a selective role in signaling by the lymphotoxin-beta receptor (LTBR; 600979). They determined that NIK is not required for signaling in response to lipopolysaccharide, IL1, and TNFA and is not a generic IKK kinase Animal model experiments

lend further support to the function of MAP3K14. The alymphoplasia (aly) mutation of mouse is autosomal recessive and characterized by the systemic absence of lymph nodes and Peyer patches and disorganized splenic and thymic structures with immunodeficiency. Shinkura et al. (1999) cloned the mouse Nik gene and determined that a G-to-A transition leads to a gly855-to-arg substitution in the C terminus of the protein, causing alymphoplasia in aly/aly mice

[7399] It is appreciated that the abovementioned animal model for MAP3K14 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7400] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7401] Shinkura, R.; Kitada, K.; Matsuda, F.; Tashiro, K.; Ikuta, K.; Suzuki, M.; Kogishi, K.; Serikawa, T.; Honjo, T. : Alymphoplasia is caused by a point mutation in the mouse gene encoding Nf-kappa-b-inducing kinase. Nature Genet. 22: 74-77, 1999. ; and

[7402] Smith, C.; Andreakos, E.; Crawley, J. B.; Brennan, F. M.; Feldmann, M.; Foxwell, B. M. J. : NF-kappa-B-inducing ki-

nase is dispensable for activation of NF-kappa-B in inflammatory setting.

[7403] Further studies establishing the function and utilities of MAP3K14 are found in John Hopkins OMIM database record ID 604655, and in cited publications numbered 7279, 1274 and 8178-7283 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355) is another VGAM55 host target gene. MPP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP2 BINDING SITE, designated SEQ ID:30081, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7404] Another function of VGAM55 is therefore inhibition of Membrane Protein, Palmitoylated 2 (MAGUK p55 subfamily member 2) (MPP2, Accession XM_008355). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with MPP2. Mucin 3B (MUC3B, Accession XM_168578) is another VGAM55 host target gene. MUC3B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MUC3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MUC3B BINDING SITE, designated SEQ ID:45258, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7405] Another function of VGAM55 is therefore inhibition of Mucin 3B (MUC3B, Accession XM_168578), a gene which provides a protective, lubricating barrier against particles and infectious agents at mucosal surfaces. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MUC3B. The function of MUC3B has been established by previous studies. The MUC3A gene (OMIM Ref. No. 158371), originally designated MUC3, encodes a trans-membrane mucin-type glycoprotein. A number of consistent single nucleotide changes were observed in different MUC3 cDNAs from a single individual, suggesting the presence of at least 3 different transcripts. Pratt et al.

(2000) presented evidence that this transcript heterogeneity is due to the existence of allelic changes and to tandem duplication of the MUC3 gene. Pratt et al. (2000) determined that the second gene, which they designated MUC3B, has the same C-terminal domain and intron-exon structure as that previously described for MUC3. The tandem repeat domain has the same amino acid consensus sequence but shows more substitutions. RT-PCR detected expression of MUC3B in fetal and adult small intestine, fetal and adult colon, and Caco-2 cells. Kyo et al. (2001) also determined that 'MUC3' consists of 2 genes, MUC3A and MUC3B, both of which encode membrane-bound mucins with 2 epidermal growth factor-like motifs and a putative transmembrane region. Fox et al. (1992) mapped the MUC3 gene (now MUC3A and MUC3B) to chromosome 7q22 by in situ hybridization.

[7406] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7407] Fox, M. F.; Lahbib, F.; Pratt, W.; Attwood, J.; Gum, J.; Kim, Y.; Swallow, D. M. : Regional localization of the intestinal mucin gene MUC3 to chromosome 7q22. *Ann. Hum. Genet.* 56: 281-287, 1992. ; and

[7408] Kyo, K.; Muto, T.; Nagawa, H.; Lathrop, G. M.; Nakamura, Y. : Associations of distinct variants of the intestinal mucin gene MUC3A with ulcerative colitis and Crohn's disease. J. Hum. G.

[7409] Further studies establishing the function and utilities of MUC3B are found in John Hopkins OMIM database record ID 605633, and in cited publications numbered 5195–519 and 4502 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nucleoporin 98kDa (NUP98, Accession NM_016320) is another VGAM55 host target gene. NUP98 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP98 BINDING SITE, designated SEQ ID:18441, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7410] Another function of VGAM55 is therefore inhibition of Nucleoporin 98kDa (NUP98, Accession NM_016320), a gene which functions in the nuclear transport of protein and RNA. Accordingly, utilities of VGAM55 include diagnosis,

prevention and treatment of diseases and clinical conditions associated with NUP98. The function of NUP98 has been established by previous studies. Nucleoporins are proteins that function in the nuclear transport of protein and RNA. Nakamura et al. (1996) showed that in 3 patients with t(7;11), the chromosome rearrangement created a genomic fusion between the HOXA9 gene (OMIM Ref. No. 142956) and the nucleoporin gene NUP98 on 11p15. Expression of Hoxa7 and Hoxa9 is activated by proviral integration in BXH2 murine myeloid leukemias; this result, combined with the mapping of the HOXA cluster to 7p15, suggested that one of the HOXA genes may be involved in the human t(7;11)(p15;p15) translocation found in some myeloid leukemia patients. The translocation produced an invariant chimeric NUP98/HOXA9 transcript containing the amino terminal half of NUP98 fused in-frame to HOXA9. These studies identified HOXA9 as an important human myeloid leukemia gene and suggested an important role for nucleoporins in human myeloid leukemia, given that a second nucleoporin, NUP214 (OMIM Ref. No. 114350), had also been implicated in human myeloid leukemia. The 11p15 gene was identified by exon trapping experiments. Borrow et al. (1996) likewise iden-

tified the HOXA9 and NUP98 genes as the parents of the fusion in t(7;11)(p15;p15) in acute myeloid leukemia of the FABM2 and M4 types. Borrow et al. (1996) suggested that the predicted NUP98/HOXA9 fusion protein may promote leukemogenesis through inhibition of HOXA9-mediated terminal differentiation and/or aberrant nucleocytoplasmic transport.

[7411] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7412] Borrow, J.; Shearman, A. M.; Stanton, V. P., Jr.; Becher, R.; Collins, T.; Williams, A. J.; Dube, I.; Katz, F.; Kwong, Y. L.; Morris, C.; Ohyashiki, K.; Toyama, K.; Rowley, J.; Housman, D. E. : The t(7;11)(p15;p15) translocation in acute myeloid leukaemia fuses the genes for nucleoporin NUP98 and class I homeoprotein HOXA9. *Nature Genet.* 12: 159–167, 1996. ; and

[7413] Nakamura, T.; Largaespada, D. A.; Lee, M. P.; Johnson, L. A.; Ohyashiki, K.; Toyama, K.; Chen, S. J.; Willman, C. L.; Chen, I.-M.; Feinberg, A. P.; Jenkins, N. A.; Copeland, N. G.; Shau.

[7414] Further studies establishing the function and utilities of NUP98 are found in John Hopkins OMIM database record

ID 601021, and in cited publications numbered 3689, 9642, 9643–9646, 2723, 9647–965 and 10957–9653 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430) is another VGAM55 host target gene. PAFAH1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAFAH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAFAH1B1 BINDING SITE, designated SEQ ID:6009, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7415] Another function of VGAM55 is therefore inhibition of Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAFAH1B1. Peripheral Myelin Protein 2 (PMP2, Accession NM_002677) is another VGAM55 host target gene. PMP2 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by PMP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMP2 BINDING SITE, designated SEQ ID:8544, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7416] Another function of VGAM55 is therefore inhibition of Peripheral Myelin Protein 2 (PMP2, Accession NM_002677), a gene which is a lipid transport protein in schwann cells. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMP2. The function of PMP2 has been established by previous studies. Myelin is a multilamellar compacted membrane structure that surrounds and insulates axons, facilitating the conduction of nerve impulses. It is composed predominantly of lipids, with proteins accounting for about 30% of its net weight. Schwann cells are responsible for myelin formation in the peripheral nervous system. Peripheral myelin protein-2 (PMP2), a small basic protein, is one of the major proteins of peripheral myelin and appears to be related to the transport

of fatty acids or the metabolism of myelin lipids. Hayasaka et al. (1991) noted that PMP2 (which they also called myelin P2 protein, MP2) was shown to have lipid-binding activity. Thus, MP2 protein may have an important role in the organization of compact myelin. Hayasaka et al. (1991) isolated a full-length cDNA of MP2 protein of peripheral myelin from a cDNA library of human fetus spinal cord. It was found to contain a 393-bp open reading frame encoding a polypeptide of 131 residues. The deduced amino acid sequence is highly homologous to myelin P2 protein from other species. Hayasaka et al. (1993) cloned the genomic PMP2 sequence, which is about 8 kb long and consists of 4 exons. All exon-intron junction sequences conform to the GT/AG rule. The 5-prime flanking region of the gene has a TA-rich element (TATA-like box) and a single defined transcription initiation site as detected by the primer extension method. By spot-blot hybridization (FISH) of flow-sorted human chromosomes and fluorescence in situ hybridization, Hayasaka et al. (1993) mapped the PMP2 gene to 8q21.3-q22.1. This is the same region as that in which the autosomal recessive form of Charcot-Marie-Tooth peroneal muscular atrophy (CMT4A; 214400) has been mapped. Thus, the

PMP2 gene was a prime candidate for the site of the mutation in that disorder.

[7417] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7418] Hayasaka, K.; Nanao, K.; Tahara, M.; Sato, W.; Takada, G.; Miura, M.; Uyemura, K. : Isolation and sequence determination of cDNA encoding P2 protein of human peripheral myelin. *Biochem. Biophys. Res. Commun.* 181: 204–207, 1991. ; and

[7419] Hayasaka, K.; Himoro, M.; Takada, G.; Takahashi, E.; Minoshima, S.; Shimizu, N. : Structure and localization of the gene encoding human peripheral myelin protein 2 (PMP2). *Genomics* 18: 244–.

[7420] Further studies establishing the function and utilities of PMP2 are found in John Hopkins OMIM database record ID 170715, and in cited publications numbered 10814–10817 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449) is another VGAM55 host target gene. RFX5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by RFX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFX5 BINDING SITE, designated SEQ ID:6046, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7421] Another function of VGAM55 is therefore inhibition of Regulatory Factor X, 5 (influences HLA class II expression) (RFX5, Accession NM_000449), a gene which activates transcription from class ii mhc promoters. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFX5. The function of RFX5 has been established by previous studies. Major histocompatibility complex (MHC) class II molecules are heterodimeric transmembrane glycoproteins consisting of alpha and beta chains. In man, there are 3 MHC class II isotypes: HLA-DR, -DP, and -DQ. MHC class II molecules play a key role in the immune system. They present exogenous antigenic peptides to the receptor of CD4+ T-helper lymphocytes, thereby triggering the antigen-specific T-cell activation events required for the initiation and sustenance of immune responses.

Durand et al. (1997) noted that the crucial role in the control of the immune response is exemplified by the finding that ectopic or aberrantly high levels of MHC class II expression is associated with autoimmune diseases, while a lack of MHC class II expression results in a severe immunodeficiency syndrome called MHC class II deficiency, or the bare lymphocyte syndrome type II (BLS; 209920). At least 4 complementation groups have been identified in B-cell lines established from patients with BLS. The molecular defect responsible for complementation group A resides in the gene encoding CIITA (MHC2TA; 600005). CIITA is a non-DNA-binding transactivator that functions as a molecular switch controlling both cell-type-specific and inducible MHC class II gene transcription. In contrast, the defects in complementation groups B, C, and D all lead to a deficiency in RFX, a nuclear protein complex that binds to the X box of MHC class II promoters (see OMIM Ref. No. RFX2; 142765). The lack of RFX binding activity in complementation group C results from mutations in the gene encoding the 75-kD subunit of RFX (Steimle et al., 1995). This gene was called RFX5 because it is the fifth member of the growing family of DNA-binding proteins sharing a novel and highly characteristic DNA-binding do-

main called the RFX motif. Nekrep et al. (2000) demonstrated a direct interaction between the C terminus of RFXAP (OMIM Ref. No. 601861) and RFXANK (OMIM Ref. No. 603200); mutant RFXAP or RFXANK proteins failed to bind. The authors found that RFX5 binds only to the RFXANK–RFXAP scaffold and not to either protein alone. However, neither the scaffold nor RFX5 alone can bind DNA. Nekrep et al. (2000) concluded that the binding of the RFXANK–RFXAP scaffold to RFX5 leads to a conformational change in the latter that exposes the DNA-binding domain of RFX5. The DNA-binding domain of RFX5 anchors the RFX complex to MHC class II X and S promoter boxes. Another part of the RFX5 protein interacts with MHC2TA. The authors pointed out that mutation of either protein in complementation group B or group D of BLS patients prevents its binding to the other protein, explaining why MHC class II promoters are bare in the bare lymphocyte syndrome.

[7422] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7423] Durand, B.; Sperisen, P.; Emery, P.; Barras, E.; Zufferey, M.; Mach, B.; Reith, W. : RFXAP, a novel subunit of the RFX

DNA binding complex is mutated in MHC class II deficiency. EMBO J. 16: 1045–1055, 1997. ; and

[7424] Nekrep, N.; Jabrane–Ferrat, N.; Peterlin, B. M. : Mutations in the bare lymphocyte syndrome define critical steps in the assembly of the regulatory factor X complex. Molec. Cell Biol. 2.

[7425] Further studies establishing the function and utilities of RFX5 are found in John Hopkins OMIM database record ID 601863, and in cited publications numbered 753, 5800, 8320, 5807, 8319, 626 and 12618 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ring Finger Protein 4 (RNF4, Accession NM_002938) is another VGAM55 host target gene. RNF4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF4 BINDING SITE, designated SEQ ID:8839, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7426] Another function of VGAM55 is therefore inhibition of Ring Finger Protein 4 (RNF4, Accession NM_002938). Ac–

cordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF4. Sal-like 1 (Drosophila) (SALL1, Accession NM_002968) is another VGAM55 host target gene. SALL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SALL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SALL1 BINDING SITE, designated SEQ ID:8878, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7427] Another function of VGAM55 is therefore inhibition of Sal-like 1 (Drosophila) (SALL1, Accession NM_002968). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SALL1. Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544) is another VGAM55 host target gene. TAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TAP2 BINDING SITE, designated SEQ ID:6142, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7428] Another function of VGAM55 is therefore inhibition of Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544), a gene which is involved in the transport of antigens from the cytoplasm to a membrane-bound compartment for association with mhc class i molecules. Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAP2. The function of TAP2 has been established by previous studies. Various studies have identified genes within the major histocompatibility complex (MHC) that play a role in presentation of antigenic peptides to T cells. RING4 (TAP1), a gene within the human MHC class II region, was found to have sequence homology with members of the ABC (ATP-binding cassette) transporter superfamily. Powis et al. (1992) reported the nucleotide sequence of RING11, a second ABC transporter gene located approximately 7 kb telomeric to RING4. RING11, or TAP2, was found to be gamma-interferon (OMIM Ref. No. 147570) inducible, a property

shared with other genes involved in antigen presentation. A comparison between the predicted amino acid sequences of RING11 and RING4 showed strong homology. Powis et al. (1992) proposed that the 2 gene products form a heterodimer that transports peptides from the cytoplasm into the endoplasmic reticulum. They identified 2 RING11 alleles that differ in the length of their derived protein sequence by 17 amino acids. The more common of these alleles had a frequency of 79% in a Caucasoid population. Both TAP1 and TAP2 polypeptides possess a nucleotide-binding domain (NBD). Karttunen et al. (2001) presented biochemical and functional evidence that the NBDs of TAP1 and TAP2 are nonequivalent. Photolabeling experiments with 8-azido-ATP demonstrated a cooperative interaction between the 2 NBDs that can be stimulated by peptide. The substitution of key lysine residues in the Walker A motifs of TAP1 and TAP2 suggested that TAP1-mediated ATP hydrolysis is not essential for peptide translocation but that TAP2-mediated ATP hydrolysis is critical, not only for translocation, but for peptide binding.

[7429] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [7430] Karttunen, J. T.; Lehner, P. J.; Gupta, S. S.; Hewitt, E. W.; Cresswell, P. : Distinct functions and cooperative interaction of the subunits of the transporter associated with antigen processing (TAP). Proc. Nat. Acad. Sci. 98: 7431–7436, 2001. ; and
- [7431] Powis, S. H.; Mockridge, I.; Kelly, A.; Kerr, L.–A.; Glynn, R.; Gileadi, U.; Beck, S.; Trowsdale, J. : Polymorphism in a second ABC transporter gene located within the class II region.
- [7432] Further studies establishing the function and utilities of TAP2 are found in John Hopkins OMIM database record ID 170261, and in cited publications numbered 1945, 1948–1951, 194 and 1952 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Usher Syndrome 3A (USH3A, Accession NM_052995) is another VGAM55 host target gene. USH3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USH3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USH3A BINDING SITE, designated SEQ ID:27560, to the nucleotide sequence of VGAM55 RNA, herein designated

VGAM RNA, also designated SEQ ID:2766.

[7433] Another function of VGAM55 is therefore inhibition of Usher Syndrome 3A (USH3A, Accession NM_052995). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USH3A. 24432 (Accession NM_022914) is another VGAM55 host target gene. 24432 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by 24432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 24432 BINDING SITE, designated SEQ ID:23225, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7434] Another function of VGAM55 is therefore inhibition of 24432 (Accession NM_022914). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 24432. BOP (Accession XM_097915) is another VGAM55 host target gene. BOP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BOP, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BOP BINDING SITE, designated SEQ ID:41210, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7435] Another function of VGAM55 is therefore inhibition of BOP (Accession XM_097915). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BOP. Chromosome 5 Open Reading Frame 7 (C5orf7, Accession XM_033576) is another VGAM55 host target gene. C5orf7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf7 BINDING SITE, designated SEQ ID:31942, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7436] Another function of VGAM55 is therefore inhibition of Chromosome 5 Open Reading Frame 7 (C5orf7, Accession XM_033576). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with C5orf7. Chromosome 6 Open Reading Frame 26 (C6orf26, Accession NM_025259) is another VGAM55 host target gene. C6orf26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf26 BINDING SITE, designated SEQ ID:24928, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7437] Another function of VGAM55 is therefore inhibition of Chromosome 6 Open Reading Frame 26 (C6orf26, Accession NM_025259). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf26. Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444) is another VGAM55 host target gene. CHRAC1 BINDING SITE1 and CHRAC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CHRAC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of CHRAC1 BINDING SITE1 and CHRAC1 BINDING SITE2, designated SEQ ID:18902 and SEQ ID:18903 respectively, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7438] Another function of VGAM55 is therefore inhibition of Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRAC1. DT1P1A10 (Accession XM_029187) is another VGAM55 host target gene.

DT1P1A10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DT1P1A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DT1P1A10 BINDING SITE, designated SEQ ID:30859, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7439] Another function of VGAM55 is therefore inhibition of DT1P1A10 (Accession XM_029187). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with DT1P1A10. FK506 Binding Protein 4, 59kDa (FKBP4, Accession NM_002014) is another VGAM55 host target gene. FKBP4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FKBP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP4 BINDING SITE, designated SEQ ID:7754, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7440] Another function of VGAM55 is therefore inhibition of FK506 Binding Protein 4, 59kDa (FKBP4, Accession NM_002014). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKBP4. FLJ11539 (Accession NM_024748) is another VGAM55 host target gene. FLJ11539 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11539 BINDING SITE, designated SEQ

ID:24086, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7441] Another function of VGAM55 is therefore inhibition of FLJ11539 (Accession NM_024748). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11539. FLJ14735 (Accession NM_032832) is another VGAM55 host target gene. FLJ14735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14735 BINDING SITE, designated SEQ ID:26607, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7442] Another function of VGAM55 is therefore inhibition of FLJ14735 (Accession NM_032832). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14735. FLJ14950 (Accession NM_032865) is another VGAM55 host target gene. FLJ14950 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ14950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14950 BINDING SITE, designated SEQ ID:26677, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7443] Another function of VGAM55 is therefore inhibition of FLJ14950 (Accession NM_032865). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14950. FLJ20079 (Accession NM_017656) is another VGAM55 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19177, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7444] Another function of VGAM55 is therefore inhibition of

FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. FLJ21596 (Accession NM_024823) is another VGAM55 host target gene. FLJ21596 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21596 BINDING SITE, designated SEQ ID:24214, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7445] Another function of VGAM55 is therefore inhibition of FLJ21596 (Accession NM_024823). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21596. FLJ22195 (Accession NM_022758) is another VGAM55 host target gene. FLJ22195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ22195 BINDING SITE, designated SEQ ID:22997, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7446] Another function of VGAM55 is therefore inhibition of FLJ22195 (Accession NM_022758). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22195. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130) is another VGAM55 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLPH3 BINDING SITE, designated SEQ ID:22689, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7447] Another function of VGAM55 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with GOLPH3. KIAA0295 (Accession XM_042833) is another VGAM55 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33779, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7448] Another function of VGAM55 is therefore inhibition of KIAA0295 (Accession XM_042833). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. KIAA0599 (Accession XM_085127) is another VGAM55 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37855, to the

nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7449] Another function of VGAM55 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA0825 (Accession XM_027906) is another VGAM55 host target gene. KIAA0825 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0825, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0825 BINDING SITE, designated SEQ ID:30594, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7450] Another function of VGAM55 is therefore inhibition of KIAA0825 (Accession XM_027906). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0825. KIAA1030 (Accession XM_167789) is another VGAM55 host target gene. KIAA1030 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1030, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1030 BINDING SITE, designated SEQ ID:44822, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7451] Another function of VGAM55 is therefore inhibition of KIAA1030 (Accession XM_167789). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1030. KIAA1126 (Accession XM_050325) is another VGAM55 host target gene. KIAA1126 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1126 BINDING SITE, designated SEQ ID:35610, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7452] Another function of VGAM55 is therefore inhibition of KIAA1126 (Accession XM_050325). Accordingly, utilities

of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1126. KIAA1464 (Accession XM_043069) is another VGAM55 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33887, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7453] Another function of VGAM55 is therefore inhibition of KIAA1464 (Accession XM_043069). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1464. KIAA1535 (Accession XM_086565) is another VGAM55 host target gene. KIAA1535 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1535 BINDING SITE, designated SEQ ID:38767, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7454] Another function of VGAM55 is therefore inhibition of KIAA1535 (Accession XM_086565). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1535. KIAA1536 (Accession NM_020898) is another VGAM55 host target gene. KIAA1536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1536 BINDING SITE, designated SEQ ID:21923, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7455] Another function of VGAM55 is therefore inhibition of KIAA1536 (Accession NM_020898). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1536. KIAA1655 (Accession XM_039442) is another VGAM55 host target gene. KIAA1655 BINDING SITE is

HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33084, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7456] Another function of VGAM55 is therefore inhibition of KIAA1655 (Accession XM_039442). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1655. KIAA1805 (Accession XM_086976) is another VGAM55 host target gene. KIAA1805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1805 BINDING SITE, designated SEQ ID:38999, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7457] Another function of VGAM55 is therefore inhibition of

KIAA1805 (Accession XM_086976). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1805. Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM_031988) is another VGAM55 host target gene. MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP2K6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP2K6 BINDING SITE1 and MAP2K6 BINDING SITE2, designated SEQ ID:25701 and SEQ ID:8642 respectively, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7458] Another function of VGAM55 is therefore inhibition of Mitogen-activated Protein Kinase Kinase 6 (MAP2K6, Accession NM_031988). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP2K6. Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540) is another VGAM55 host target gene. NCOA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by NCOA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCOA2 BINDING SITE, designated SEQ ID:13294, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7459] Another function of VGAM55 is therefore inhibition of Nuclear Receptor Coactivator 2 (NCOA2, Accession NM_006540). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCOA2. Solute Carrier Family 38, Member 5 (SLC38A5, Accession NM_033518) is another VGAM55 host target gene. SLC38A5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC38A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC38A5 BINDING SITE, designated SEQ ID:27296, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7460] Another function of VGAM55 is therefore inhibition of So-

lute Carrier Family 38, Member 5 (SLC38A5, Accession NM_033518). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC38A5. Target of Myb1 (chicken) (TOM1, Accession NM_005488) is another VGAM55 host target gene. TOM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TOM1 BINDING SITE, designated SEQ ID:11985, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7461] Another function of VGAM55 is therefore inhibition of Target of Myb1 (chicken) (TOM1, Accession NM_005488). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOM1. Tweety Homolog 2 (Drosophila) (TTYH2, Accession NM_032646) is another VGAM55 host target gene. TTYH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TTYH2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TTYH2 BINDING SITE, designated SEQ ID:26379, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7462] Another function of VGAM55 is therefore inhibition of Tweety Homolog 2 (Drosophila) (TTYH2, Accession NM_032646). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TTYH2. UDP Glycosyltransferase 2 Family, Polypeptide B10 (UGT2B10, Accession NM_001075) is another VGAM55 host target gene. UGT2B10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UGT2B10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UGT2B10 BINDING SITE, designated SEQ ID:6736, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7463] Another function of VGAM55 is therefore inhibition of UDP

Glycosyltransferase 2 Family, Polypeptide B10 (UGT2B10, Accession NM_001075). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UGT2B10. Zinc Finger Protein 238 (ZNF238, Accession NM_006352) is another VGAM55 host target gene. ZNF238 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF238 BINDING SITE, designated SEQ ID:13043, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7464] Another function of VGAM55 is therefore inhibition of Zinc Finger Protein 238 (ZNF238, Accession NM_006352). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF238. LOC144893 (Accession XM_096687) is another VGAM55 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40462, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7465] Another function of VGAM55 is therefore inhibition of LOC144893 (Accession XM_096687). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC147042 (Accession XM_097167) is another VGAM55 host target gene. LOC147042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147042 BINDING SITE, designated SEQ ID:40787, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7466] Another function of VGAM55 is therefore inhibition of LOC147042 (Accession XM_097167). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC147042. LOC147093 (Accession XM_097184) is another VGAM55 host target gene. LOC147093 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147093 BINDING SITE, designated SEQ ID:40805, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7467] Another function of VGAM55 is therefore inhibition of LOC147093 (Accession XM_097184). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147093. LOC147645 (Accession XM_085831) is another VGAM55 host target gene. LOC147645 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147645, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147645 BINDING SITE, designated SEQ ID:38360, to

the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7468] Another function of VGAM55 is therefore inhibition of LOC147645 (Accession XM_085831). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147645. LOC150299 (Accession XM_097869) is another VGAM55 host target gene. LOC150299 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150299, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150299 BINDING SITE, designated SEQ ID:41181, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7469] Another function of VGAM55 is therefore inhibition of LOC150299 (Accession XM_097869). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150299. LOC151647 (Accession XM_087261) is another VGAM55 host target gene. LOC151647 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC151647, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151647 BINDING SITE, designated SEQ ID:39157, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7470] Another function of VGAM55 is therefore inhibition of LOC151647 (Accession XM_087261). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151647. LOC152274 (Accession XM_087418) is another VGAM55 host target gene. LOC152274 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152274, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152274 BINDING SITE, designated SEQ ID:39236, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7471] Another function of VGAM55 is therefore inhibition of LOC152274 (Accession XM_087418). Accordingly, utilities

of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152274. LOC152275 (Accession XM_098186) is another VGAM55 host target gene. LOC152275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152275 BINDING SITE, designated SEQ ID:41459, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7472] Another function of VGAM55 is therefore inhibition of LOC152275 (Accession XM_098186). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152275. LOC152313 (Accession XM_098190) is another VGAM55 host target gene. LOC152313 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC152313 BINDING SITE, designated SEQ ID:41473, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7473] Another function of VGAM55 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC153196 (Accession XM_098323) is another VGAM55 host target gene. LOC153196 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153196 BINDING SITE, designated SEQ ID:41592, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7474] Another function of VGAM55 is therefore inhibition of LOC153196 (Accession XM_098323). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153196. LOC157909 (Accession XM_088419) is another VGAM55 host target gene. LOC157909 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157909 BINDING SITE, designated SEQ ID:39679, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7475] Another function of VGAM55 is therefore inhibition of LOC157909 (Accession XM_088419). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157909. LOC158450 (Accession XM_088580) is another VGAM55 host target gene. LOC158450 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158450 BINDING SITE, designated SEQ ID:39844, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7476] Another function of VGAM55 is therefore inhibition of

LOC158450 (Accession XM_088580). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158450. LOC158504 (Accession XM_088591) is another VGAM55 host target gene. LOC158504 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158504 BINDING SITE, designated SEQ ID:39855, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7477] Another function of VGAM55 is therefore inhibition of LOC158504 (Accession XM_088591). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158504. LOC200205 (Accession XM_114152) is another VGAM55 host target gene. LOC200205 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC200205 BINDING SITE, designated SEQ ID:42735, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7478] Another function of VGAM55 is therefore inhibition of LOC200205 (Accession XM_114152). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200205. LOC200261 (Accession XM_114172) is another VGAM55 host target gene. LOC200261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200261 BINDING SITE, designated SEQ ID:42749, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7479] Another function of VGAM55 is therefore inhibition of LOC200261 (Accession XM_114172). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200261. LOC222662 (Accession XM_167086) is an-

other VGAM55 host target gene. LOC222662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222662 BINDING SITE, designated SEQ ID:44602, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7480] Another function of VGAM55 is therefore inhibition of LOC222662 (Accession XM_167086). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222662. LOC254556 (Accession XM_170588) is another VGAM55 host target gene. LOC254556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254556 BINDING SITE, designated SEQ ID:45392, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7481] Another function of VGAM55 is therefore inhibition of LOC254556 (Accession XM_170588). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254556. LOC254707 (Accession XM_173687) is another VGAM55 host target gene. LOC254707 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254707 BINDING SITE, designated SEQ ID:46554, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7482] Another function of VGAM55 is therefore inhibition of LOC254707 (Accession XM_173687). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254707. LOC257612 (Accession XM_175270) is another VGAM55 host target gene. LOC257612 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257612, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257612 BINDING SITE, designated SEQ ID:46740, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7483] Another function of VGAM55 is therefore inhibition of LOC257612 (Accession XM_175270). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257612. LOC51652 (Accession NM_016079) is another VGAM55 host target gene. LOC51652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51652 BINDING SITE, designated SEQ ID:18152, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7484] Another function of VGAM55 is therefore inhibition of LOC51652 (Accession NM_016079). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC51652. LOC90520 (Accession XM_032277) is another VGAM55 host target gene. LOC90520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90520 BINDING SITE, designated SEQ ID:31631, to the nucleotide sequence of VGAM55 RNA, herein designated VGAM RNA, also designated SEQ ID:2766.

[7485] Another function of VGAM55 is therefore inhibition of LOC90520 (Accession XM_032277). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90520. LOC91050 (Accession XM_035703) is another VGAM55 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32339, to the nucleotide sequence of VGAM55 RNA, herein designated

VGAM RNA, also designated SEQ ID:2766.

[7486] Another function of VGAM55 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities of VGAM55 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 56 (VGAM56) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7487] VGAM56 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM56 was detected is described hereinabove with reference to Figs. 1–8.

[7488] VGAM56 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7489] VGAM56 gene encodes a VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM56 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM56 precursor RNA is designated SEQ ID:42, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:42 is located at position 116893 relative to the genome of Invertebrate Iridescent Virus 6.

[7490] VGAM56 precursor RNA folds onto itself, forming VGAM56 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7491] An enzyme complex designated DICER COMPLEX, `dices` the VGAM56 folded precursor RNA into VGAM56 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM56 RNA is designated SEQ ID:2767, and is provided hereinbelow with reference to the sequence listing part.

[7492] VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM56 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[7493] VGAM56 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM56 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM56 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7494] The complementary binding of VGAM56 RNA, herein designated VGAM RNA, to host target binding sites on VGAM56 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM56 host target RNA into VGAM56 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7495] It is appreciated that VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM56 host target genes. The mRNA of each one of this plurality of VGAM56 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM56 RNA, herein designated VGAM RNA, and which when bound by VGAM56 RNA causes inhibition of translation of respective one or more VGAM56 host target proteins.

[7496] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM56 gene, herein designated VGAM GENE, on one or more VGAM56 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7497] It is yet further appreciated that a function of VGAM56 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM56 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM56 correlate with, and may be deduced from, the identity of the host target genes which VGAM56 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7498] Nucleotide sequences of the VGAM56 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM56 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM56 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM56 are further described hereinbelow with reference to Table 1.

[7499] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM56 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM56 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7500] As mentioned hereinabove with reference to Fig. 1, a function of VGAM56 gene, herein designated VGAM is inhibition of expression of VGAM56 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM56 correlate with, and may be deduced from, the identity of the target genes which VGAM56 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7501] Chromosome 9 Open Reading Frame 14 (C9orf14, Accession XM_098859) is a VGAM56 host target gene. C9orf14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C9orf14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf14 BINDING SITE, designated SEQ ID:41908, to the nucleotide sequence of VGAM56 RNA, herein designated VGAM RNA, also designated SEQ ID:2767.

[7502] A function of VGAM56 is therefore inhibition of Chromosome 9 Open Reading Frame 14 (C9orf14, Accession XM_098859). Accordingly, utilities of VGAM56 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with C9orf14. LOC143187 (Accession NM_145206) is another VGAM56 host target gene. LOC143187 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143187 BINDING SITE, designated SEQ ID:29745, to the nucleotide sequence of VGAM56 RNA, herein designated VGAM RNA, also designated SEQ ID:2767.

[7503] Another function of VGAM56 is therefore inhibition of LOC143187 (Accession NM_145206). Accordingly, utilities of VGAM56 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143187. LOC158332 (Accession XM_088554) is another VGAM56 host target gene. LOC158332 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC158332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158332 BINDING SITE, designated SEQ ID:39824, to

the nucleotide sequence of VGAM56 RNA, herein designated VGAM RNA, also designated SEQ ID:2767.

[7504] Another function of VGAM56 is therefore inhibition of LOC158332 (Accession XM_088554). Accordingly, utilities of VGAM56 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158332. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 57 (VGAM57) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7505] VGAM57 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM57 was detected is described hereinabove with reference to Figs. 1–8.

[7506] VGAM57 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7507] VGAM57 gene encodes a VGAM57 precursor RNA, herein

designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM57 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM57 precursor RNA is designated SEQ ID:43, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:43 is located at position 14382 relative to the genome of Invertebrate Iridescent Virus 6.

[7508] VGAM57 precursor RNA folds onto itself, forming VGAM57 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7509] An enzyme complex designated DICER COMPLEX, `dices` the VGAM57 folded precursor RNA into VGAM57 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM57 RNA is designated SEQ ID:2768, and is provided hereinbelow with reference to the sequence listing part.

[7510] VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM57 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7511] VGAM57 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM57 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, desig-

nated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM57 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7512] The complementary binding of VGAM57 RNA, herein designated VGAM RNA, to host target binding sites on VGAM57 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM57 host target RNA into VGAM57 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7513] It is appreciated that VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM57 host target genes. The mRNA of

each one of this plurality of VGAM57 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM57 RNA, herein designated VGAM RNA, and which when bound by VGAM57 RNA causes inhibition of translation of respective one or more VGAM57 host target proteins.

[7514] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM57 gene, herein designated VGAM GENE, on one or more VGAM57 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7515] It is yet further appreciated that a function of VGAM57 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM57 correlate with, and may be deduced from, the identity of the host target genes which VGAM57 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7516] Nucleotide sequences of the VGAM57 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM57 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM57 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM57 are further described hereinbelow with reference to Table 1.

[7517] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM57 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM57 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[7518] As mentioned hereinabove with reference to Fig. 1, a function of VGAM57 gene, herein designated VGAM is inhibition of expression of VGAM57 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM57 correlate with, and may be deduced from, the identity of the target genes which VGAM57 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7519] Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082) is a VGAM57 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5533, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7520] A function of VGAM57 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with CKN1. Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is another VGAM57 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10699, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7521] Another function of VGAM57 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 has been established by previous studies. The Drosophila dishevelled gene (*dsh*) encodes a cytoplasmic phosphoprotein (Klingensmith et al., 1994) that regulates cell proliferation, acting as a transducer molecule for developmental processes, including segmentation and neuroblast specification. Pizzuti et al. (1996) noted that *dsh* is required for

the function of the wingless gene product wg, a segment polarity gene homologous to the mammalian protooncogene WNT1 (OMIM Ref. No. 164820). Pizzuti et al. (1996) reported the isolation and chromosomal mapping of 2 human dsh homologs, designated DVL1 (OMIM Ref. No. 601365) and DVL3 by them. The human dsh homologs were isolated from a fetal brain cDNA library. DVL3 encodes a predicted 716-amino acid polypeptide that shows 74% nucleotide homology with human DVL1 and 71% homology with the mouse Dvl1 gene. DVL1 and DVL3 share 64% amino acid identity. Pizzuti et al. (1996) reported that homology is particularly high in the N-terminal region and that there is more divergence in the C-terminal regions. PCR carried out using DNA from rodent human somatic cell hybrids and DVL3 specific primers led to the assignment of DVL3 to human chromosome 3. Pizzuti et al. (1996) regionally assigned DVL3 to band 3q27 using fluorescence in situ hybridization. Hybridization of poly(A) mRNA with the DVL3 cDNA revealed a 2.9-kb transcript with abundant expression in skeletal muscle, pancreas and heart. They also detected 5.9-kb and 5.0-kb transcripts in skeletal muscle, adult liver, adult heart, pancreas, and placenta. The 5.9-kb form was abundant in fe-

tal tissues but the 5.0-kb form was absent from these tissues. Pizzuti et al. (1996) noted that Charcot-Marie-Tooth type 2B (OMIM Ref. No. 600882) maps to chromosome 3q. Bui et al. (1997) also isolated human DVL3, which shares 98% amino acid identity with mouse Dvl3 and 49% with *Drosophila dsh*. The authors confirmed the chromosomal localization at 3p27. Semenov and Snyder (1997) isolated 3 human genes encoding proteins homologous to *Drosophila dsh*. The cDNA sequence of DVL3 reported by Semenov and Snyder (1997) differs from the previously reported sequences deposited in GenBank. Bui et al. (1997) detected expression of DVL3 mRNA in B cells, breast, kidney, bladder, endometrium, and 2 primary endometrial cultures. It was detected equally in normal human breast tissues and tumors and in colorectal samples of normal tissues, polyps, and tumors.

[7522] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7523] Pizzuti, A.; Amati, F.; Calabrese, G.; Mari, A.; Colosimo, A; Silani, V.; Giardino, L.; Ratti, A.; Penso, D.; Calza, L.; Palka, G.; Scarlato, G.; Novelli, G.; Dallapiccola, B. : cDNA characterization and chromosomal mapping of two human ho-

mologs of the Drosophila dishevelled polarity gene. Hum. Molec. Genet. 5: 953–958, 1996. ; and

[7524] Semenov, M. V.; Snyder, M. : Human dishevelled genes constitute a DHR-containing multigene family. Genomics 42: 302–310, 1997.

[7525] Further studies establishing the function and utilities of DVL3 are found in John Hopkins OMIM database record ID 601368, and in cited publications numbered 9864–6902 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epidermal Growth Factor (beta-urogastrone) (EGF, Accession NM_001963) is another VGAM57 host target gene. EGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGF BINDING SITE, designated SEQ ID:7688, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7526] Another function of VGAM57 is therefore inhibition of Epidermal Growth Factor (beta-urogastrone) (EGF, Accession NM_001963), a gene which stimulates the growth of epi-

dermal and epithelial tissues and of some fibroblasts in cell culture. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGF. The function of EGF has been established by previous studies. During the immediate-early response of mammalian cells to mitogens, histone H3 (see OMIM Ref. No. 601128) is rapidly and transiently phosphorylated by one or more kinases. Sassone-Corsi et al. (1999) demonstrated that EGF-stimulated phosphorylation of H3 requires RSK2 (OMIM Ref. No. 300075), a member of the pp90(RSK) family of kinases implicated in growth control. Looking for the genetic factors that mediate susceptibility to, and outcome of, sporadic malignant melanoma, Shahbazi et al. (2002) focused on epidermal growth factor because of its role in mitogenesis. They tested for genetic polymorphisms in EGF in 135 white European patients with malignant melanoma and in 99 healthy white European controls. They identified a single-nucleotide substitution, G to A, at position 61 of the EGF gene. Frequencies of the A and G alleles of EGF were 56% and 44%, respectively, in controls. Cells from individuals homozygous for the 61A allele produced significantly less EGF than cells from 61G homozygotes or A/G

heterozygotes. Compared with the A/A genotype, G/G was significantly associated with risk of malignant melanoma (odds ratio 4.9, p less than 0.0001).

[7527] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7528] Sassone-Corsi, P.; Mizzen, C. A.; Cheung, P.; Crosjo, C.; Monaco, L.; Jacquot, S.; Hanauer, A.; Allis, C. D. : Requirement of Rsk-2 for epidermal growth factor-activated phosphorylation of histone H3. Science 285: 886-891, 1999. ; and

[7529] Shahbazi, M.; Pravica, V.; Nasreen, N.; Fakhoury, H.; Fryer, A. A.; Strange, R. C.; Hutchinson, P. E.; Osborne, J. E.; Lear, J. T.; Smith, A. G.; Hutchinson, I. V. : Association between.

[7530] Further studies establishing the function and utilities of EGF are found in John Hopkins OMIM database record ID 131530, and in cited publications numbered 4631-4644 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ellis Van Creveld Syndrome (EVC, Accession NM_014556) is another VGAM57 host target gene. EVC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by EVC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVC BINDING SITE, designated SEQ ID:15885, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7531] Another function of VGAM57 is therefore inhibition of Ellis Van Creveld Syndrome (EVC, Accession NM_014556). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVC. Eve, Even-skipped Homeo Box Homolog 1 (Drosophila) (EVX1, Accession NM_001989) is another VGAM57 host target gene. EVX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EVX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVX1 BINDING SITE, designated SEQ ID:7713, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7532] Another function of VGAM57 is therefore inhibition of Eve,

Even-skipped Homeo Box Homolog 1 (Drosophila) (EVX1, Accession NM_001989). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVX1. Fanconi Anemia, Complementation Group E (FANCE, Accession NM_021922) is another VGAM57 host target gene. FANCE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCE BINDING SITE, designated SEQ ID:22447, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7533] Another function of VGAM57 is therefore inhibition of Fanconi Anemia, Complementation Group E (FANCE, Accession NM_021922), a gene which is a possible regulator of lymphocyte and platelet function. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCE. The function of FANCE has been established by previous studies. A number sign (#) is used with this entry because Fanconi anemia is caused by mutation in 1 of the Fanconi

anemia complementation group genes: FANCA (OMIM Ref. No. 607139), FANCB (OMIM Ref. No. 227660), FANCC (OMIM Ref. No. 227645), FANCD1 (OMIM Ref. No. 605724), FANCD2 (OMIM Ref. No. 227646), FANCE (OMIM Ref. No. 600901), FANCF (OMIM Ref. No. 603467), FANCG (OMIM Ref. No. 602956). The previously designated FANCH complementation group (Joenje et al., 1997) was found by Joenje et al. (2000) to be the same as FANCA. Joenje et al. (1995) presented evidence for a fifth subtype of Fanconi anemia, designated group E. Buchwald (1995) stated that 6 of 31 patients (12.7%) could be classified as group E. The FACE group is defined as being different from groups A (OMIM Ref. No. 227650), B (OMIM Ref. No. 227660), C (OMIM Ref. No. 227645), and D (OMIM Ref. No. 227646) and may itself be heterogeneous.

[7534] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7535] Joenje, H.; Lo Ten Foe, J. R.; Oostra, A. B.; van Berkel, C. G. M.; Rooimans, M. A.; Schroeder-Kurth, T.; Wegner, R.-D.; Gille, J. J. P.; Buchwald, M.; Arwert, F. : Classification of Fanconi anemia patients by complementation analysis: evidence for a fifth genetic subtype. Blood 86: 2156–2160,

1995. ; and

[7536] Buchwald, M. : Complementation groups: one or more per gene? Nature Genet. 11: 228–230, 1995.

[7537] Further studies establishing the function and utilities of FANCE are found in John Hopkins OMIM database record ID 600901, and in cited publications numbered 9588, 9367, 9368, 943 and 9605–9606 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801) is another VGAM57 host target gene. FKBP1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FKBP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKBP1A BINDING SITE, designated SEQ ID:6472, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7538] Another function of VGAM57 is therefore inhibition of FK506 Binding Protein 1A, 12kDa (FKBP1A, Accession NM_000801), a gene which FK506-binding protein 1A. Accordingly, utilities of VGAM57 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with FKBP1A. The function of FKBP1A has been established by previous studies. FK506, a macrolide, is a powerful immunosuppressant like cyclosporin A (CsA). CsA and FK506 are chemically distinct but have remarkably similar immunosuppressive action, although FK506 is many times more potent than CsA. The action of CsA may be mediated through cyclophilin (OMIM Ref. No. 123840), which is identical to peptidyl–prolyl cis–trans isomerase (OMIM Ref. No. PPlase), and the immunosuppressive action of CsA in T cells may be mediated through inhibition of this enzyme activity. FK506–binding protein (FKBP) also has peptidyl–prolyl cis–trans isomerase enzymatic activity; however, whereas cyclophilin binds to, and is inhibited by, CsA but does not recognize FK506, the converse holds for FKBP. Since the 2 drugs have essentially equivalent action on T lymphocytes, it may be that they act through distinct pathways but their mode of action converges on PPlase activities. Maki et al. (1990) isolated and sequenced DNA coding for FKBP from human peripheral blood T lymphocytes by using mixed 20–mer oligonucleotide probes synthesized on the basis of the sequence of bovine FKBP. They found an open reading frame encoding 108 amino

acid residues, the first 40 of which were identical to those of the bovine sequence. Analysis showed no significant sequence similarity to any other known protein, including cyclophilin. Southern blot analysis of human genomic DNA digested with different restriction enzymes suggested the existence of only a few copies of the FKBP gene. This is in contrast to the results indicating as many as 20 copies of the cyclophilin gene as well as possible pseudogenes in the mammalian genome. Standaert et al. (1990) likewise isolated a cDNA for FKBP and reported the derived amino acid sequence. The human FKBP cDNA sequence showed significant similarity to an open reading frame in the genome of *Neisseria meningitidis*. Wang et al. (1994) reported that in a yeast genetic screen, FKBP1 interacted with various type I receptors, including the TGF- β type I receptor (OMIM Ref. No. 190181). Deletion, point mutation, and co-immunoprecipitation studies demonstrated the specificity of this interaction, and competitive binding assays indicated that the type I receptor may be a natural ligand for FKBP1. Wang et al. (1994) concluded that FKBP1 may play a role in type I receptor-mediated signaling. Peattie et al. (1994) identified 3 distinct mRNAs for FKBP12, designated A, B, and C, that result from differen-

tial splicing or polyadenylation. All 3 encode the same protein sequence. The ryanodine receptor on the sarcoplasmic reticulum is the major source of calcium required for cardiac muscle excitation–contraction coupling. The channel is a tetramer comprised of 4 RYR2 (OMIM Ref. No. 180902) polypeptides and 4 FK506–binding proteins (OMIM Ref. No. FKBP1A). Marx et al. (2000) showed that protein kinase A (PKA; OMIM Ref. No. 176911) phosphorylation of RYR2 dissociates FKBP1A and regulates the channel open probability. Using cosedimentation and coimmunoprecipitation, the authors defined a macromolecular complex comprised of RYR2, FKBP1A, PKA, the protein phosphatases PP1 (see OMIM Ref. No. 603771) and PP2A (see OMIM Ref. No. 603113), and an anchoring protein, AKAP6 (OMIM Ref. No. 604691). In failing human hearts, Marx et al. (2000) showed that RYR2 is PKA hyperphosphorylated, resulting in defective channel function due to increased sensitivity to calcium–induced activation. To define the functions of FKBP12 in vivo, Shou et al. (1998) generated mutant mice deficient in FKBP12 using embryonic stem (ES) cell technology. FKBP12–deficient mice had normal skeletal muscle but had severe dilated cardiomyopathy and ventricular septal defects that mim–

icked a human congenital heart disorder, namely non-compaction of left ventricular myocardium (see OMIM Ref. No. 300183 for an X-linked form of myocardial noncompaction). About 9% of the mutants exhibited exencephaly secondary to a defect in neural tube closure. Physiologic studies demonstrated that FKBP12 is dispensable for TGF-beta-mediated signaling, but modulates the calcium release activity of both skeletal and cardiac ryanodine receptors.

[7539] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7540] Standaert, R. F.; Galat, A.; Verdine, G. L.; Schreiber, S. L. : Molecular cloning and overexpression of the human FK506-binding protein FKBP. Nature 346: 671-674, 1990.
; and

[7541] Shou, W.; Aghdasi, B.; Armstrong, D. L.; Guo, Q.; Bao, S.; Charng, M.-J.; Mathews, L. M.; Schneider, M. D.; Hamilton, S. L.; Matzuk, M. M. : Cardiac defects and altered ryanodine recepto.

[7542] Further studies establishing the function and utilities of FKBP1A are found in John Hopkins OMIM database record ID 186945, and in sited publications numbered

10032–1003 and 10271–10040 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069) is another VGAM57 host target gene. GNAI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI1 BINDING SITE, designated SEQ ID:7843, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7543] Another function of VGAM57 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069), a gene which is involved as modulators or transducers in various transmembrane signaling systems. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI1. The function of GNAI1 has been established by previous studies. The G proteins that mediate hormone responses can be divided into 2 broad cat-

egories according to their interaction with the bacterial toxins from *Vibrio cholera* and *Bordetella pertussis*. Those G proteins whose primary function is to stimulate adenylate kinase are substrates for ATP-ribosylation by cholera toxin, whereas those involved in hormonal inhibition of adenylate kinase and in regulation of other plasma membrane enzymes are substrates for pertussis toxin. The G protein family of signal transducers includes 5 heterotrimers, which are most clearly distinguished by their different alpha chains; they have virtually identical beta chains and similar gamma chains. The 5 heterotrimers are Gs (OMIM Ref. No. 139320) and Gi, the stimulatory and inhibitory GTP-binding regulators of adenylate cyclase; Go, a protein abundant in brain (see OMIM Ref. No. 139311); and transducin 1 (OMIM Ref. No. 139330) and transducin 2, proteins involved in phototransduction in retinal rods and cones, respectively. Sullivan et al. (1986) used a cDNA encoding bovine alpha chain of transducin 1 to isolate and sequence murine cDNAs for alpha(s) and alpha(i). Homologies and differences among the deduced amino acid sequences of the G protein and transducin alpha chains pointed to specific regions that may interact with guanine nucleotides, receptors, effector enzymes,

and the G protein beta-gamma complex. Studying cDNA clones, Bray et al. (1987) concluded that there are at least 2 classes of alpha(i) mRNA, one represented by brain tissue and another represented by monocytes. Suki et al. (1987) concluded that the human genome contains at least 3 nonallelic genes for alpha-i-type subunits of G protein. Neer et al. (1987) cloned and characterized cDNA encoding the predominant alpha(i) of brain, together with a very similar cDNA that encodes another putative G protein, alpha(h). The former gene was found to be located on human chromosome 7 by Southern blot analysis of DNA from mouse-human hybrid cell lines. Bloch et al. (1988) mapped the GNAI1 gene to 7q21 by in situ hybridization. They confirmed the regional location by studying human/mouse somatic cell hybrid lines containing portions of human chromosome 7. This location is near that of cystic fibrosis (CF; 219700), a disorder that is accompanied by hyporesponsiveness to beta-adrenergic medications. Bloch et al. (1988) excluded the GNAI1 locus as a 'candidate gene' for CF by showing that the GNAI1 gene is located closer to the centromere of chromosome 7 than are 2 marker loci that flank the CF locus. The relative position of these loci was determined by Southern analysis

of hybrid cells containing various portions of chromosome 7. By screening human genomic libraries with rat cDNAs for Gi-alpha as probes, Itoh et al. (1988) isolated 3 genes for the alpha subunit. The second and third are composed of 8 coding exons and 7 introns and possess completely identical exon-intron organization. Southern blot analysis indicated that a single copy of each of the 3 genes is present in the haploid human genome. Blatt et al. (1988) mapped GNAI1 to chromosome 7 by hybridization of cDNA clones with DNA from human-mouse somatic cell hybrids. By the study of restriction fragment length variation (RFLV) in an interspecific backcross between C57BL/6J and *Mus spretus* mice, Wilkie et al. (1992) demonstrated that the corresponding gene is located on mouse chromosome 5.

[7544] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7545] Bloch, D. B.; Bloch, K. D.; Iannuzzi, M.; Collins, F. S.; Neer, E. J.; Seidman, J. G.; Morton, C. C. : The gene for the alpha-i-1 subunit of human guanine nucleotide binding protein maps near the cystic fibrosis locus. *Am. J. Hum. Genet.* 42: 884-888, 1988. ; and

[7546] Wilkie, T. M.; Gilbert, D. J.; Olsen, A. S.; Chen, X.-N.; Amatruda, T. T.; Korenberg, J. R.; Trask, B. J.; de Jong, P.; Reed, R. R.; Simon, M. I.; Jenkins, N. A.; Copeland, N. G. : Evolu.

[7547] Further studies establishing the function and utilities of GNAI1 are found in John Hopkins OMIM database record ID 139310, and in cited publications numbered 4744-3603, 2187, 3604-360 and 2186 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Golgi Complex Associated Protein 1, 60kDa (GOCAP1, Accession NM_022735) is another VGAM57 host target gene. GOCAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOCAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOCAP1 BINDING SITE, designated SEQ ID:22938, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7548] Another function of VGAM57 is therefore inhibition of Golgi Complex Associated Protein 1, 60kDa (GOCAP1, Accession NM_022735). Accordingly, utilities of VGAM57 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with GOCAP1. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 2 (MLLT2, Accession NM_005935) is another VGAM57 host target gene. MLLT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT2 BINDING SITE, designated SEQ ID:12568, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7549] Another function of VGAM57 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 2 (MLLT2, Accession NM_005935), a gene which is a Putative transcription factor. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT2. The function of MLLT2 has been established by previous studies. Nakamura et al. (1993) found that the gene on chromosome 4q21 that is fused with the ALL1 gene in patients with acute lym-

phoblastic leukemia and translocation t(4;11)(q21;q23) and the gene on chromosome 9 that is fused with the ALL1 gene on chromosome 11 in patients with leukemia and the t(9;11)(p22;q23) show high sequence homology with the ENL gene on chromosome 19 which is fused to the ALL1 gene in patients with leukemia and the translocation t(11;19)(q23;p13). They found further that the protein products of the AF4, AF9 (MLLT3), and ENL (MLLT1) genes contained nuclear targeting sequences as well as serine-rich and proline-rich regions. Stretches abundant in basic amino acids were also present in the 3 proteins. These results indicated that the different proteins fused to ALL1 polypeptides in leukemia provide similar functional domains. Uckun et al. (1998) analyzed bone marrow leukemic cells of 17 infants and 127 children with newly diagnosed acute lymphatic leukemia (ALL), as well as fetal liver and bone marrow and normal infant bone marrow samples for the presence of a t(4;11) translocation, using standard cytogenetic techniques and expression of an MLL-AF4 fusion transcript by standard RT-PCR assays as well as nested RT-PCR that is 100-fold more sensitive than the standard RT-PCR. Overall, 9 of the 17 infants and 17 of 127 noninfant pediatric ALL patients were positive

for expression of MLL–AF4 fusion transcripts. None of the MLL–AF4(+) cases were positive for E2A–PBX1 (147141; 176310) or BCR–ABL (151410; 189980) fusion transcript expression. Although 8 of 9 MLL–AF4(+) infants had cytogenetically detectable t(4;11) translocation, 15 of the 17 MLL–AF4(+) noninfants were t(4;11) negative. Infants with MLL–AF4(+) ALL had poor outcomes, whereas noninfant fusion–gene–positive, translocation–negative patients has favorable outcomes similar to MLL–AF4(–) patients. Notably, MLL–AF4 transcripts also were detected by nested RT–PCR in 4 of 16 fetal bone marrows, 5 of 13 fetal livers, and 1 of 6 normal infant bone marrows, but not in any of the 44 remission bone marrow specimens from pediatric ALL patients. These results represented unprecedented evidence that MLL–AF4 fusion transcripts can be present in normal hematopoietic cells, indicating that their expression is insufficient for leukemic transformation of normal lymphocyte precursors.

[7550] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7551] Nakamura, T.; Alder, H.; Gu, Y.; Prasad, R.; Canaani, O.; Kamada, N.; Gale, R. P.; Lange, B.; Crist, W. M.; Nowell, P.

C.; Croce, C. M.; Canaani, E. : Genes on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia share sequence homology and/or common motifs. Proc. Nat. Acad. Sci. 90: 4631–4635, 1993. ; and

[7552] Uckun, F. M.; Herman–Hatten, K.; Crotty, M.–L.; Sensel, M. G.; Sather, H. N.; Tuel–Ahlgren, L.; Sarquis, M. B.; Bostrom, B.; Nachman, J. B.; Steinherz, P. G.; Gaynon, P. S.; Heerema, N.

[7553] Further studies establishing the function and utilities of MLLT2 are found in John Hopkins OMIM database record ID 159557, and in cited publications numbered 3275–3276, 1843–184 and 3277 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nidogen (enactin) (NID, Accession NM_002508) is another VGAM57 host target gene. NID BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NID, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NID BINDING SITE, designated SEQ ID:8340, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7554] Another function of VGAM57 is therefore inhibition of Nidogen (enactin) (NID, Accession NM_002508). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NID. 5'-nucleotidase, Ecto (CD73) (NT5E, Accession NM_002526) is another VGAM57 host target gene. NT5E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NT5E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NT5E BINDING SITE, designated SEQ ID:8364, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7555] Another function of VGAM57 is therefore inhibition of 5'-nucleotidase, Ecto (CD73) (NT5E, Accession NM_002526). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NT5E. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily C, Member 1 (SMARCC1, Accession NM_003074) is another VGAM57 host target gene. SMARCC1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by SMARCC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCC1 BINDING SITE, designated SEQ ID:9041, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7556] Another function of VGAM57 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily C, Member 1 (SMARCC1, Accession NM_003074), a gene which is involved in chromatin remodeling. Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCC1. The function of SMARCC1 has been established by previous studies. Chromatin is actively remodeled during development. Chromatin remodeling of certain genes appears to precede their transcriptional activation. In yeast, the multisubunit SWI/SNF complex is thought to be responsible for chromatin remodeling. Wang et al. (1996) isolated an analogous SWI/SNF complex from human YT cells. They found that the resultant complexes are com-

posed of 9 to 12 polypeptides, which they termed BAFs (for BRG1-associated factors). Wang et al. (1996) isolated BAF155 from a human Jurkat T-cell cDNA library. This gene encodes a polypeptide of 1,104 amino acids, and is homologous both to the yeast SWI3 gene and to BAF170, another of the proteins in this chromatin remodeling complex (OMIM Ref. No. 601734). SWI3, BAF155, and BAF170 all contain a predicted leucine zipper region (a dimerization motif for a variety of transcription factors) and a myb-like tryptophan-repeat domain. Western blot analysis and EST database analysis revealed that BAF155 is expressed in many tissues

[7557] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7558] Ring, H. Z.; Vameghi-Meyers, V.; Wang, W.; Crabtree, G. R.; Francke, U. : Five SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin (SMARC) genes are dispersed in the human genome. *Genomics* 51: 140-143, 1998. ; and

[7559] Wang, W.; Xue, Y.; Zhou, S.; Kuo, A.; Cairns, B. R.; Crabtree, G. R. : Diversity and specialization of mammalian SWI/SNF complexes. *Genes Dev.* 10: 2117-2130, 1996.

[7560] Further studies establishing the function and utilities of SMARCC1 are found in John Hopkins OMIM database record ID 601732, and in cited publications numbered 9322–9323 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169) is another VGAM57 host target gene. SUFU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUFU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUFU BINDING SITE, designated SEQ ID:18256, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7561] Another function of VGAM57 is therefore inhibition of Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUFU. ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069) is another VGAM57 host target gene. ATP1B4 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by ATP1B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B4 BINDING SITE, designated SEQ ID:14325, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7562] Another function of VGAM57 is therefore inhibition of ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B4. COE2 (Accession XM_034639) is another VGAM57 host target gene. COE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COE2 BINDING SITE, designated SEQ ID:32128, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7563] Another function of VGAM57 is therefore inhibition of

COE2 (Accession XM_034639). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COE2. DKFZP564O0423 (Accession XM_166254) is another VGAM57 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44066, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7564] Another function of VGAM57 is therefore inhibition of DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. FLJ10420 (Accession NM_018090) is another VGAM57 host target gene. FLJ10420 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10420 BINDING SITE, designated SEQ ID:19856, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7565] Another function of VGAM57 is therefore inhibition of FLJ10420 (Accession NM_018090). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10420. FLJ11117 (Accession NM_018329) is another VGAM57 host target gene. FLJ11117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11117 BINDING SITE, designated SEQ ID:20327, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7566] Another function of VGAM57 is therefore inhibition of FLJ11117 (Accession NM_018329). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11117. FLJ14457 (Accession NM_032788) is another VGAM57

host target gene. FLJ14457 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14457 BINDING SITE, designated SEQ ID:26542, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7567] Another function of VGAM57 is therefore inhibition of FLJ14457 (Accession NM_032788). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14457. FLJ23231 (Accession NM_025079) is another VGAM57 host target gene. FLJ23231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23231 BINDING SITE, designated SEQ ID:24679, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7568] Another function of VGAM57 is therefore inhibition of FLJ23231 (Accession NM_025079). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23231. FLJ31978 (Accession NM_144669) is another VGAM57 host target gene. FLJ31978 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31978, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31978 BINDING SITE, designated SEQ ID:29490, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7569] Another function of VGAM57 is therefore inhibition of FLJ31978 (Accession NM_144669). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31978. FLJ32334 (Accession NM_144565) is another VGAM57 host target gene. FLJ32334 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32334 BINDING SITE, designated SEQ ID:29367, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7570] Another function of VGAM57 is therefore inhibition of FLJ32334 (Accession NM_144565). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32334. GBTS1 (Accession NM_145173) is another VGAM57 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29729, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7571] Another function of VGAM57 is therefore inhibition of GBTS1 (Accession NM_145173). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1.

ITM3 (Accession NM_030926) is another VGAM57 host target gene. ITM3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITM3 BINDING SITE, designated SEQ ID:25195, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7572] Another function of VGAM57 is therefore inhibition of ITM3 (Accession NM_030926). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITM3. KIAA0350 (Accession XM_028332) is another VGAM57 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30671, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2768.

[7573] Another function of VGAM57 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA0663 (Accession NM_014827) is another VGAM57 host target gene. KIAA0663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0663 BINDING SITE, designated SEQ ID:16811, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7574] Another function of VGAM57 is therefore inhibition of KIAA0663 (Accession NM_014827). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0663. KIAA0795 (Accession NM_025010) is another VGAM57 host target gene. KIAA0795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0795, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0795 BINDING SITE, designated SEQ ID:24585, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7575] Another function of VGAM57 is therefore inhibition of KIAA0795 (Accession NM_025010). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0795. KIAA1010 (Accession XM_050742) is another VGAM57 host target gene. KIAA1010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1010 BINDING SITE, designated SEQ ID:35668, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7576] Another function of VGAM57 is therefore inhibition of KIAA1010 (Accession XM_050742). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1010. KIAA1210 (Accession XM_172801) is another VGAM57 host target gene. KIAA1210 BINDING SITE1 and KIAA1210 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1210, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1210 BINDING SITE1 and KIAA1210 BINDING SITE2, designated SEQ ID:46085 and SEQ ID:46086 respectively, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7577] Another function of VGAM57 is therefore inhibition of KIAA1210 (Accession XM_172801). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1210. KIAA1775 (Accession NM_033100) is another VGAM57 host target gene. KIAA1775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1775 BINDING SITE, designated SEQ ID:26941, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7578] Another function of VGAM57 is therefore inhibition of KIAA1775 (Accession NM_033100). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1775. KIAA1829 (Accession XM_030378) is another VGAM57 host target gene. KIAA1829 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1829 BINDING SITE, designated SEQ ID:31029, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7579] Another function of VGAM57 is therefore inhibition of KIAA1829 (Accession XM_030378). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1829. Protocadherin 10 (PCDH10, Accession

NM_032961) is another VGAM57 host target gene.

PCDH10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PCDH10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH10 BINDING SITE, designated SEQ ID:26769, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7580] Another function of VGAM57 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM_032961). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. TRIP-Br2 (Accession NM_014755) is another VGAM57 host target gene. TRIP-Br2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIP-Br2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIP-Br2 BINDING SITE, designated SEQ ID:16491, to the nucleotide sequence of VGAM57 RNA, herein designated

VGAM RNA, also designated SEQ ID:2768.

[7581] Another function of VGAM57 is therefore inhibition of TRIP-Br2 (Accession NM_014755). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIP-Br2. LOC115073 (Accession XM_055193) is another VGAM57 host target gene. LOC115073 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115073 BINDING SITE, designated SEQ ID:36236, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7582] Another function of VGAM57 is therefore inhibition of LOC115073 (Accession XM_055193). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115073. LOC128344 (Accession XM_059234) is another VGAM57 host target gene. LOC128344 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128344, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128344 BINDING SITE, designated SEQ ID:36922, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7583] Another function of VGAM57 is therefore inhibition of LOC128344 (Accession XM_059234). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128344. LOC143452 (Accession XM_084522) is another VGAM57 host target gene. LOC143452 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143452 BINDING SITE, designated SEQ ID:37622, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7584] Another function of VGAM57 is therefore inhibition of LOC143452 (Accession XM_084522). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC143452. LOC144308 (Accession XM_096575) is another VGAM57 host target gene. LOC144308 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144308 BINDING SITE, designated SEQ ID:40407, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7585] Another function of VGAM57 is therefore inhibition of LOC144308 (Accession XM_096575). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144308. LOC152573 (Accession XM_087488) is another VGAM57 host target gene. LOC152573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152573 BINDING SITE, designated SEQ ID:39288, to

the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7586] Another function of VGAM57 is therefore inhibition of LOC152573 (Accession XM_087488). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152573. LOC201194 (Accession XM_117061) is another VGAM57 host target gene. LOC201194 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201194 BINDING SITE, designated SEQ ID:43217, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7587] Another function of VGAM57 is therefore inhibition of LOC201194 (Accession XM_117061). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201194. LOC219899 (Accession XM_166173) is another VGAM57 host target gene. LOC219899 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC219899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219899 BINDING SITE, designated SEQ ID:43993, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7588] Another function of VGAM57 is therefore inhibition of LOC219899 (Accession XM_166173). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219899. LOC253019 (Accession XM_170907) is another VGAM57 host target gene. LOC253019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253019 BINDING SITE, designated SEQ ID:45666, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7589] Another function of VGAM57 is therefore inhibition of LOC253019 (Accession XM_170907). Accordingly, utilities

of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253019. LOC253975 (Accession XM_171130) is another VGAM57 host target gene. LOC253975 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253975 BINDING SITE, designated SEQ ID:45933, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7590] Another function of VGAM57 is therefore inhibition of LOC253975 (Accession XM_171130). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253975. LOC257486 (Accession XM_045029) is another VGAM57 host target gene. LOC257486 BINDING SITE1 and LOC257486 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC257486, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LOC257486 BINDING SITE1 and LOC257486 BINDING SITE2, designated SEQ ID:34323 and SEQ ID:34324 respectively, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7591] Another function of VGAM57 is therefore inhibition of LOC257486 (Accession XM_045029). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257486. LOC90170 (Accession XM_029589) is another VGAM57 host target gene. LOC90170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90170 BINDING SITE, designated SEQ ID:30909, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7592] Another function of VGAM57 is therefore inhibition of LOC90170 (Accession XM_029589). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90170. LOC91208 (Accession XM_036935) is another VGAM57 host target gene. LOC91208 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91208, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91208 BINDING SITE, designated SEQ ID:32521, to the nucleotide sequence of VGAM57 RNA, herein designated VGAM RNA, also designated SEQ ID:2768.

[7593] Another function of VGAM57 is therefore inhibition of LOC91208 (Accession XM_036935). Accordingly, utilities of VGAM57 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91208. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 58 (VGAM58) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7594] VGAM58 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM58 was detected is described hereinabove with reference to Figs. 1–8.

[7595] VGAM58 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7596] VGAM58 gene encodes a VGAM58 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM58 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM58 precursor RNA is designated SEQ ID:44, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:44 is located at position 76117 relative to the genome of Invertebrate Iridescent Virus 6.

[7597] VGAM58 precursor RNA folds onto itself, forming VGAM58 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first

half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7598] An enzyme complex designated DICER COMPLEX, `dices` the VGAM58 folded precursor RNA into VGAM58 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM58 RNA is designated SEQ ID:2769, and is provided hereinbelow with reference to the sequence listing part.

[7599] VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM58 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7600] VGAM58 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM58 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM58 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM58 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7601] The complementary binding of VGAM58 RNA, herein designated VGAM RNA, to host target binding sites on VGAM58 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM58 host target RNA into VGAM58 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7602] It is appreciated that VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM58 host target genes. The mRNA of each one of this plurality of VGAM58 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM58 RNA, herein designated VGAM RNA, and which when bound by VGAM58 RNA causes inhibition of translation of respective one or more VGAM58 host target proteins.

[7603] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM58 gene, herein designated VGAM GENE, on one or more VGAM58 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7604] It is yet further appreciated that a function of VGAM58 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM58 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM58 correlate with, and may be deduced from, the identity of the host target genes which VGAM58 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7605] Nucleotide sequences of the VGAM58 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM58 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM58 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM58 are further described hereinbelow with reference to Table 1.

[7606] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM58 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM58 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7607] As mentioned hereinabove with reference to Fig. 1, a function of VGAM58 gene, herein designated VGAM is inhibition of expression of VGAM58 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM58 correlate with, and may be deduced from, the identity of the target genes which VGAM58 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7608] ETR101 (Accession XM_051364) is a VGAM58 host target gene. ETR101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ETR101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of ETR101 BINDING SITE, designated SEQ ID:35829, to the nucleotide sequence of VGAM58 RNA, herein designated VGAM RNA, also designated SEQ ID:2769.

[7609] A function of VGAM58 is therefore inhibition of ETR101 (Accession XM_051364). Accordingly, utilities of VGAM58 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ETR101. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 59 (VGAM59) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7610] VGAM59 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM59 was detected is described hereinabove with reference to Figs. 1–8.

[7611] VGAM59 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7612] VGAM59 gene encodes a VGAM59 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM59 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM59 precursor RNA is designated SEQ ID:45, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:45 is located at position 64386 relative to the genome of Invertebrate Iridescent Virus 6.

[7613] VGAM59 precursor RNA folds onto itself, forming VGAM59 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7614] An enzyme complex designated DICER COMPLEX, `dices` the VGAM59 folded precursor RNA into VGAM59 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM59 RNA is designated SEQ ID:2770, and is provided hereinbelow with reference to the sequence listing part.

[7615] VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM59 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7616] VGAM59 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM59 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration,

Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM59 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7617] The complementary binding of VGAM59 RNA, herein designated VGAM RNA, to host target binding sites on VGAM59 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM59 host target RNA into VGAM59 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7618] It is appreciated that VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM59 host target genes. The mRNA of each one of this plurality of VGAM59 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM59 RNA, herein designated VGAM RNA, and which when bound by VGAM59 RNA causes inhibition of translation of respective one or more VGAM59 host target proteins.

[7619] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM59 gene, herein designated VGAM GENE, on one or more VGAM59 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective:

Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7620] It is yet further appreciated that a function of VGAM59 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM59 correlate with, and may be deduced from, the identity of the host target genes which VGAM59 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7621] Nucleotide sequences of the VGAM59 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM59 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM59 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM59 are further described hereinbelow with reference to Table 1.

[7622] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM59 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM59 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[7623] As mentioned hereinabove with reference to Fig. 1, a function of VGAM59 gene, herein designated VGAM is inhibition of expression of VGAM59 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM59 correlate with, and may be deduced from, the identity of the target genes which VGAM59 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7624] Doublesex and Mab-3 Related Transcription Factor 1 (DMRT1, Accession NM_021951) is a VGAM59 host target gene. DMRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMRT1 BINDING SITE, designated SEQ ID:22481, to the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA, also designated SEQ ID:2770.

[7625] A function of VGAM59 is therefore inhibition of Doublesex and Mab-3 Related Transcription Factor 1 (DMRT1, Acces-

sion NM_021951), a gene which May be involved in male sexual development. Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMRT1. The function of DMRT1 has been established by previous studies. Shan et al. (2000) reviewed the accumulating evidence that haploinsufficiency of a dosage-sensitive gene(s) in 9p24.3 is responsible for the failure of testicular development and feminization in XY patients with monosomy for 9p. They used molecular cytogenetic methods to characterize the sex-reversing 9p deletions in 2 XY females. FISH with YACs from the critical 9p region containing the DMRT1 gene proved to be a fast and reliable assay for patient screening. Comparative YAC mapping on great ape and Old and New World monkey chromosomes demonstrated that the critical region was moved from an interstitial position on the ancestral primate chromosome to a very subtelomeric position in chimpanzee and humans by a pericentric inversion(s). Pathologic 9p rearrangements may be the consequence of an evolutionary chromosome breakpoint in close proximity to the sex-reversal region. Muroya et al. (2000) reported clinical and molecular findings in 5 karyotypic males (cases 1–5) and 1 karyotypic

female (OMIM Ref. No. case 6) with distal 9p monosomy. Cases 1–3 and 6 had female external genitalia, case 4 showed ambiguous external genitalia, and case 5 exhibited male external genitalia with left cryptorchidism and right intrascrotal testis. Gonadal explorations at gonadectomy in case 3 and 4 revealed that case 3 had left streak gonad and right agonadism, and case 4 had bilateral hypoplastic testes. Endocrine studies in cases 1–4 and 6 showed that cases 1, 3, and 6 had definite primary hypogonadism, with basal FSH (see OMIM Ref. No. 118850) levels of 54, 39, and 41 IU/L, respectively, whereas case 2 with severe malnutrition was unremarkable for the baseline values, and case 4 had fairly good testicular function. FISH and microsatellite analyses demonstrated that all cases had hemizygosity of the 9p sex-determining region distal to D9S1779, with loss of DMRT1 and DMRT2 from the abnormal chromosome 9. Sequence analysis in cases 1–4 and 6 showed that they had normal sequences of each exon of DMRT1 and the DM domain of DMRT2 on the normal chromosome 9, and that cases 1–4 had normal SRY sequences. The authors concluded that the results provide further support for the presence of a sex-determining gene(s) on distal 9p and favor the possibility

of DMRT1 and/or DMRT2 being the sex-determining gene(s). They inferred that haploinsufficiency of the 9p sex-determining gene(s) primarily hinders the formation of indifferent gonad, leading to various degrees of defective testis formation in karyotypic males and impaired ovary function in karyotypic females.

[7626] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7627] Muroya, K.; Okuyama, T.; Goishi, K.; Ogiso, Y.; Fukuda, S.; Kameyama, J.; Sato, H.; Suzuki, Y.; Terasaki, H.; Gomyo, H.; Wakui, K.; Fukushima, Y.; Ogata, T. : Sex-determining gene(s) on distal 9p: clinical and molecular studies in six cases. J. Clin. Endocr. Metab. 85: 3094–3100, 2000. ; and

[7628] Shan, Z.; Zabel, B.; Trautmann, U.; Hillig, U.; Ottolenghi, C.; Wang, Y.; Haaf, T. : FISH mapping of the sex-reversal region on human chromosome 9p in two XY females and in primates. Eu.

[7629] Further studies establishing the function and utilities of DMRT1 are found in John Hopkins OMIM database record ID 602424, and in cited publications numbered 122 and 8908–8914 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calpain 6

(CAPN6, Accession NM_014289) is another VGAM59 host target gene. CAPN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN6 BINDING SITE, designated SEQ ID:15567, to the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA, also designated SEQ ID:2770.

[7630] Another function of VGAM59 is therefore inhibition of Calpain 6 (CAPN6, Accession NM_014289). Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN6. FLJ13769 (Accession NM_025012) is another VGAM59 host target gene. FLJ13769 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13769 BINDING SITE, designated SEQ ID:24592, to the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA,

also designated SEQ ID:2770.

[7631] Another function of VGAM59 is therefore inhibition of FLJ13769 (Accession NM_025012). Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13769. FLJ22167 (Accession NM_024533) is another VGAM59 host target gene. FLJ22167 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22167, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22167 BINDING SITE, designated SEQ ID:23740, to the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA, also designated SEQ ID:2770.

[7632] Another function of VGAM59 is therefore inhibition of FLJ22167 (Accession NM_024533). Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22167. H-plk (Accession NM_015852) is another VGAM59 host target gene. H-plk BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by H-plk, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H-plk BINDING SITE, designated SEQ ID:17983, to the nucleotide sequence of VGAM59 RNA, herein designated VGAM RNA, also designated SEQ ID:2770.

[7633] Another function of VGAM59 is therefore inhibition of H-plk (Accession NM_015852). Accordingly, utilities of VGAM59 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H-plk. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 60 (VGAM60) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7634] VGAM60 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM60 was detected is described hereinabove with reference to Figs. 1–8.

[7635] VGAM60 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM60 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7636] VGAM60 gene encodes a VGAM60 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM60 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM60 precursor RNA is designated SEQ ID:46, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:46 is located at position 157538 relative to the genome of Invertebrate Iridescent Virus 6.

[7637] VGAM60 precursor RNA folds onto itself, forming VGAM60 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7638] An enzyme complex designated DICER COMPLEX, `dices` the VGAM60 folded precursor RNA into VGAM60 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM60 RNA is designated SEQ ID:2771, and is provided hereinbelow with reference to the sequence listing part.

[7639] VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM60 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7640] VGAM60 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM60 RNA is an accurate or a partial in-

versed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM60 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7641] The complementary binding of VGAM60 RNA, herein designated VGAM RNA, to host target binding sites on VGAM60 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM60 host target RNA into VGAM60 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7642] It is appreciated that VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM60 host target genes. The mRNA of each one of this plurality of VGAM60 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM60 RNA, herein designated VGAM RNA, and which when bound by VGAM60 RNA causes inhibition of translation of respective one or more VGAM60 host target proteins.

[7643] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM60 gene, herein designated VGAM GENE, on one or more VGAM60 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7644] It is yet further appreciated that a function of VGAM60 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM60 correlate with, and may be deduced from, the identity of the host target genes which VGAM60 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7645] Nucleotide sequences of the VGAM60 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM60 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM60 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM60 are further described hereinbelow with reference to Table 1.

[7646] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM60 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM60 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7647] As mentioned hereinabove with reference to Fig. 1, a function of VGAM60 gene, herein designated VGAM is inhibition of expression of VGAM60 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM60 correlate with, and may be deduced from, the identity of the target genes which VGAM60 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7648] Cadherin 6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM_004932) is a VGAM60 host target gene. CDH6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH6 BINDING SITE, designated SEQ ID:11373, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7649] A function of VGAM60 is therefore inhibition of Cadherin

6, Type 2, K-cadherin (fetal kidney) (CDH6, Accession NM_004932), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH6. The function of CDH6 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate cell-cell binding in a homophilic manner. They play key roles in morphogenesis and in the maintenance of orderly structures such as epithelium, and may be involved in the metastasis and invasion of cancer. Mature cadherin proteins are composed of a large N-terminal extracellular domain, a single membrane-spanning domain, and a small C-terminal cytoplasmic domain. The extracellular domain consists of 5 subdomains, each containing a cadherin motif, and appears to determine the specificity of the homophilic cell adhesion activity of the cadherin; the amino acid sequence of the cytoplasmic domain is highly conserved among cadherins. CLONING By PCR using degenerate oligonucleotides based on highly conserved sequences of the cadherin cytoplasmic domain, followed by screening of a human fetal brain cDNA library, Suzuki et al. (1991) isolated a partial cDNA encoding

CDH6. Using this partial CDH6 cDNA to screen a human hepatocellular carcinoma cell cDNA library, Shimoyama et al. (1995) cloned a full-length CDH6 cDNA. The deduced 790-amino acid CDH6 protein contains a signal sequence, prosequence, extracellular domain, transmembrane sequence, and cytoplasmic domain. The predicted 737-amino acid mature CDH6 protein has 97% amino acid similarity with rat K-cadherin, 64% with human CDH12 (OMIM Ref. No. 600562), and 60% with human CDH8 (OMIM Ref. No. 603008) and CDH11 (OMIM Ref. No. 600023). Northern blot analysis detected multiple CDH6 transcripts in a variety of normal human tissues, with highest levels in kidney, brain, and cerebellum; no expression was found in liver, heart, or colonic mucosa. Four of 6 hepatocellular carcinoma cell lines and 3 of 4 renal carcinoma cell lines showed strong expression of CDH6 transcripts. Among small cell lung carcinoma lines, all 11 CDH6-positive lines were of the classic type, whereas all 4 CDH6-negative lines were of the variant type.

[7650] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7651] Shimoyama, Y.; Gotoh, M.; Terasaki, T.; Kitajima, M.; Hiro-

hashi, S. : Isolation and sequence analysis of human cadherin-6 complementary DNA for the full coding sequence and its expression in human carcinoma cells. Cancer Res. 55: 2206-2211, 1995. ; and

[7652] Suzuki, S.; Sano, K.; Tanihara, H. : Diversity of the cadherin family: evidence for eight new cadherins in nervous tissue. Cell Regul. 2: 261-270, 1991.

[7653] Further studies establishing the function and utilities of CDH6 are found in John Hopkins OMIM database record ID 603007, and in cited publications numbered 587 and 5878 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pro-melanin-concentrating Hormone-like 1 (PMCHL1, Accession NM_031887) is another VGAM60 host target gene. PMCHL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMCHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMCHL1 BINDING SITE, designated SEQ ID:25632, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7654] Another function of VGAM60 is therefore inhibition of Pro-melanin-concentrating Hormone-like 1 (PMCHL1, Accession NM_031887). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMCHL1. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155) is another VGAM60 host target gene. SERPINB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB9 BINDING SITE, designated SEQ ID:10368, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7655] Another function of VGAM60 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155), a gene which may be a serpin serine protease inhibitor that interacts with granzyme B (GZMB). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with SERPINB9. The function of SERPINB9 has been established by previous studies. Serine proteinase inhibitors (serpins) are a large superfamily of proteins which bind to and inactivate serine proteinases. These interactions are involved in many cellular processes including coagulation, fibrinolysis, complement fixation, matrix remodeling, and apoptosis. Sprecher et al. (1995) isolated PI8 (OMIM Ref. No. 601697) and PI9 cDNAs from a human placenta cDNA library. The authors found that PI9 encodes a 374-amino acid polypeptide with over 60% identity with PI6. Northern blot analysis by Sprecher et al. (1995) demonstrated that PI9 is expressed as 2 transcripts of 3.4 and 4.4 kb which were detected in greatest abundance in lung and placenta. In searching for serpins related to PI6, Sun et al. (1996) isolated and cloned PI9 from human bone marrow mRNA using a PCR cloning strategy. They confirmed that the sequence of PI9 is closely related to PI6 (OMIM Ref. No. 173321) and the viral serpin CrmA. Sun et al. (1996) showed that PI9 forms an SDS-resistant complex with granzyme B (OMIM Ref. No. 123910), suggesting that these 2 proteins may form a physiologically significant serpin-serine proteinase interaction. Sun et al. (1996) also observed that PI9 was expressed in immune tissue,

including lymphocytes, natural killer cell leukemia cell lines, and peripheral blood mononuclear cells. Sun et al. (1996) used fractionation experiments to show that PI9 is localized to the cytosol, in a separate subcellular compartment from granzyme B. PI9 was identified as an endogenous inhibitor of caspase-1 (OMIM Ref. No. 147678). Krieg et al. (2001) reported that PI9 mRNA and protein are rapidly and directly induced by estrogen in human liver cells. Using transient transfections to assay PI9 promoter truncations and mutations, they showed that this strong estrogen induction is mediated by a unique downstream estrogen responsive unit (ERU) approximately 200 nucleotides downstream of the transcription start site. They also demonstrated estrogen-dependent binding of ER to the cellular PI9 promoter. The ERU consists of an imperfect estrogen response element (ERE) palindrome immediately adjacent to a direct repeat containing two consensus ERE half-sites separated by 13 nucleotides (DR13). In transient transfections, all 4 of the ERE half-sites in the imperfect ERE and in the DR13 were important for estrogen inducibility. They concluded that a direct repeat can function with an imperfect ERE palindrome to confer estrogen inducibility on a native gene, which extends the

repertoire of DNA sequences able to function as EREs.

[7656] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7657] Sun, J.; Bird, C. H.; Sutton, V.; McDonald, L.; Coughlin, P. B.; De Jong, T. A.; Trapani, J. A.; Bird, P. I. : A cytosolic granzyme B inhibitor related to the viral apoptotic regulator cytokine response modifier A is present in cytotoxic lymphocytes. J. Biol. Chem. 271: 27802–27809, 1996. ; and

[7658] Krieg, S. A.; Krieg, A. J.; Shapiro, D. J. : A unique downstream estrogen responsive unit mediates estrogen induction of proteinase inhibitor–9, a cellular inhibitor of IL–1–beta–conver.

[7659] Further studies establishing the function and utilities of SERPINB9 are found in John Hopkins OMIM database record ID 601799, and in cited publications numbered 6248–625 and 6708 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Smcx Homolog, X Chromosome (mouse) (SMCX, Accession NM_004187) is another VGAM60 host target gene. SMCX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SMCX,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMCX BINDING SITE, designated SEQ ID:10397, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7660] Another function of VGAM60 is therefore inhibition of Smcx Homolog, X Chromosome (mouse) (SMCX, Accession NM_004187), a gene which escapes X inactivation. Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMCX. The function of SMCX has been established by previous studies. Agulnik et al. (1994) cloned a gene, designated Smcx, from the mouse X chromosome by its homology to the Y-located gene Smcy. Using direct in situ hybridization, Smcx was mapped to the distal end of the mouse X chromosome (XF2–XF4) and its human homolog, SMCX, was mapped to proximal Xp (Xp11.2–p11.1). Meiotic mapping in the mouse placed Smcx in the interval between Plp and Pdha1. Agulnik et al. (1994) showed that the Smcx gene escapes X inactivation; in hamster/human hybrids, it was expressed when either an active or an inactive human X chromosome was

present. Furthermore, 2 alleles of Smcx were found to be expressed in t(16;X)16H female mice despite the intact X chromosome being inactive in all cells. Thus, Smcx is also not subject to X inactivation. Agulnik et al. (1994) stated that this was the first example in the mouse of a gene that escapes X inactivation. Brown et al. (1995) demonstrated that the DXS423E gene (OMIM Ref. No. 300040), which is also located on Xp11.22–p11.21, likewise escapes X chromosome inactivation. Thus, the DXS423E and XE169 genes define a new region in the proximal short arm of the X chromosome that is not subject to X chromosome inactivation. Lingenfelter et al. (1998) showed that Smcx is susceptible to complete X inactivation in a portion of mouse embryonic cells. Furthermore, Smcx inactivation persists in some cells at least until 13.5 days postcoitum. A highly variable Smcx expression found during mouse development progressively disappears in adult tissues where nearly equal expression between alleles is observed

[7661] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7662] Agulnik, A. I.; Mitchell, M. J.; Mattei, M.–G.; Borsani, G.; Avner, P. A.; Lerner, J. L.; Bishop, C. E. : A novel X gene

with a widely transcribed Y-linked homologue escapes X-inactivation in mouse and human. Hum. Molec. Genet. 3: 879-884, 1994. ; and

[7663] Lingenfelter, P. A.; Adler, D. A.; Poslinski, D.; Thomas, S.; Elliott, R. W.; Chapman, V. M.; Disteche, C. M. : Escape from X inactivation of Smcx is preceded by silencing during mouse deve.

[7664] Further studies establishing the function and utilities of SMCX are found in John Hopkins OMIM database record ID 314690, and in cited publications numbered 2925-292 and 7316-2929 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788) is another VGAM60 host target gene. UBE4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE4A BINDING SITE, designated SEQ ID:11193, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7665] Another function of VGAM60 is therefore inhibition of Ubiquitination Factor E4A (UFD2 homolog, yeast) (UBE4A, Accession NM_004788), a gene which binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE4A. The function of UBE4A has been established by previous studies. Ubiquitination involves a ubiquitin-activating enzyme, or E1 (see OMIM Ref. No. UBE1, 314370), a ubiquitin-conjugating enzyme, or E2 (see OMIM Ref. No. UBE2D1, 602961), and often a substrate-specific ubiquitin-protein ligase, or E3 (see OMIM Ref. No. UBE3A, 601623). Koegl et al. (1999) showed that efficient multiubiquitination necessary for proteasomal targeting of a model substrate requires an additional conjugation factor, which they referred to as E4. This protein, previously known as UFD2 in yeast, binds to the ubiquitin moieties of preformed conjugates and catalyzes ubiquitin chain assembly in conjunction with E1, E2, and E3. Protein E4 defines a novel protein family that includes the human protein KIAA0126 (first described by Nagase et al. (1995)) and the regulatory protein NOSA from Dictyostelium. Hu-

man protein KIAA0126 contains 1,073 predicted amino acid residues. In yeast, E4 activity is linked to cell survival under stress conditions, indicating that eukaryotes utilize E4-dependent proteolysis pathways for multiple cellular functions. By analysis of a human/rodent hybrid cell panel, Nagase et al. (1995) mapped the gene encoding protein KIAA0126 to chromosome 11.

[7666] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7667] Koegl, M.; Hoppe, T.; Schlenker, S.; Ulrich, H. D.; Mayer, T. U.; Jentsch, S. : A novel ubiquitination factor, E4, is involved in multiubiquitin chain assembly. Cell 96: 635-644, 1999. ; and

[7668] Nagase, T.; Seki, N.; Tanaka, A.; Ishikawa, K.; Nomura, N. : Prediction of the coding sequences of unidentified human genes. IV. The coding sequences of 40 new genes (KIAA0121-KIAA0160.

[7669] Further studies establishing the function and utilities of UBE4A are found in John Hopkins OMIM database record ID 603753, and in cited publications numbered 759 and 10969 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Fin-

ger Protein 141 (clone pHZ-44) (ZNF141, Accession NM_003441) is another VGAM60 host target gene. ZNF141 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF141, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF141 BINDING SITE, designated SEQ ID:9497, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7670] Another function of VGAM60 is therefore inhibition of Zinc Finger Protein 141 (clone pHZ-44) (ZNF141, Accession NM_003441). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF141. ATP-binding Cassette, Sub-family A (ABC1), Member 9 (ABCA9, Accession NM_080283) is another VGAM60 host target gene. ABCA9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ABCA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of ABCA9 BINDING SITE, designated SEQ ID:27828, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7671] Another function of VGAM60 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 9 (ABCA9, Accession NM_080283). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA9. KIAA0534 (Accession XM_049349) is another VGAM60 host target gene. KIAA0534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0534 BINDING SITE, designated SEQ ID:35382, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7672] Another function of VGAM60 is therefore inhibition of KIAA0534 (Accession XM_049349). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0534. KIAA1229 (Accession XM_030665) is another

VGAM60 host target gene. KIAA1229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1229 BINDING SITE, designated SEQ ID:31102, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7673] Another function of VGAM60 is therefore inhibition of KIAA1229 (Accession XM_030665). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1229. LOC129831 (Accession XM_059376) is another VGAM60 host target gene. LOC129831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129831 BINDING SITE, designated SEQ ID:36982, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7674] Another function of VGAM60 is therefore inhibition of LOC129831 (Accession XM_059376). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129831. LOC151040 (Accession XM_087082) is another VGAM60 host target gene. LOC151040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151040 BINDING SITE, designated SEQ ID:39045, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7675] Another function of VGAM60 is therefore inhibition of LOC151040 (Accession XM_087082). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151040. LOC254672 (Accession XM_170619) is another VGAM60 host target gene. LOC254672 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254672, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254672 BINDING SITE, designated SEQ ID:45399, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7676] Another function of VGAM60 is therefore inhibition of LOC254672 (Accession XM_170619). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254672. LOC90843 (Accession XM_034430) is another VGAM60 host target gene. LOC90843 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90843 BINDING SITE, designated SEQ ID:32116, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7677] Another function of VGAM60 is therefore inhibition of LOC90843 (Accession XM_034430). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC90843. LOC92568 (Accession XM_045852) is another VGAM60 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34582, to the nucleotide sequence of VGAM60 RNA, herein designated VGAM RNA, also designated SEQ ID:2771.

[7678] Another function of VGAM60 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM60 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 61 (VGAM61) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7679] VGAM61 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM61 was detected is described hereinabove with reference to Figs. 1–8.

[7680] VGAM61 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7681] VGAM61 gene encodes a VGAM61 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM61 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM61 precursor RNA is designated SEQ ID:47, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:47 is located at position 133573 relative to the genome of Invertebrate Iridescent Virus 6.

[7682] VGAM61 precursor RNA folds onto itself, forming VGAM61 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first

half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7683] An enzyme complex designated DICER COMPLEX, `dices` the VGAM61 folded precursor RNA into VGAM61 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM61 RNA is designated SEQ ID:2772, and is provided hereinbelow with reference to the sequence listing part.

[7684] VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM61 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7685] VGAM61 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM61 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM61 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM61 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7686] The complementary binding of VGAM61 RNA, herein designated VGAM RNA, to host target binding sites on VGAM61 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM61 host target RNA into VGAM61 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7687] It is appreciated that VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM61 host target genes. The mRNA of each one of this plurality of VGAM61 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM61 RNA, herein designated VGAM RNA, and which when bound by VGAM61 RNA causes inhibition of translation of respective one or more VGAM61 host target proteins.

[7688] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM61 gene, herein designated VGAM GENE, on one or more VGAM61 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7689] It is yet further appreciated that a function of VGAM61 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM61 correlate with, and may be deduced from, the identity of the host target genes which VGAM61 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7690] Nucleotide sequences of the VGAM61 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM61 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM61 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM61 are further described hereinbelow with reference to Table 1.

[7691] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM61 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM61 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7692] As mentioned hereinabove with reference to Fig. 1, a function of VGAM61 gene, herein designated VGAM is inhibition of expression of VGAM61 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM61 correlate with, and may be deduced from, the identity of the target genes which VGAM61 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7693] F-box and Leucine-rich Repeat Protein 5 (FBXL5, Accession NM_033535) is a VGAM61 host target gene. FBXL5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FBXL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of FBXL5 BINDING SITE, designated SEQ ID:27305, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7694] A function of VGAM61 is therefore inhibition of F-box and Leucine-rich Repeat Protein 5 (FBXL5, Accession NM_033535), a gene which is a putative SCF ubiquitin ligase subunit involved in protein degradation. Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXL5. The function of FBXL5 has been established by previous studies. The F box, named after cyclin F (CCNF; 600227), in which it was originally observed, is an approximately 40-amino acid motif that binds SKP1 (OMIM Ref. No. 601434). F-box proteins are components of modular E3 ubiquitin protein ligases called SCFs (SKP1, OMIM Ref. No. 603134, F-box proteins), which function in phosphorylation-dependent ubiquitination. Using a yeast 2-hybrid screen with SKP1 as bait, followed by searching sequence databases, Winston et al. (1999) and Cenciarelli et al. (1999) identified 33 mammalian and 26 human F-box proteins, respectively. These contained C termini with leucine-rich repeats (FBXLs, e.g., SKP2 (OMIM

Ref. No. 601436)), WD40 domains (FBXWs, e.g., BTRCP (OMIM Ref. No. 603482)), or no recognizable motifs (FBXOs, e.g., CCNF). Winston et al. (1999) predicted the presence of 6 leucine-rich repeats (LRRs) in FBXL5. RT-PCR analysis detected expression in all tissues tested, with highest levels in heart and pancreas.

[7695] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7696] Ilyin, G. P.; Rialland, M.; Pigeon, C.; Guguen-Guillouzo, C. : cDNA cloning and expression analysis of new members of the mammalian F-box protein family. *Genomics* 67: 40-47, 2000. ; and

[7697] Winston, J. T.; Koepp, D. M.; Zhu, C.; Elledge, S. J.; Harper, J. W. : A family of mammalian F-box proteins. *Curr. Biol.* 9: 1180-1182, 1999.

[7698] Further studies establishing the function and utilities of FBXL5 are found in John Hopkins OMIM database record ID 605655, and in cited publications numbered 40 and 8278 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069) is another

VGAM61 host target gene. GNAI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNAI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNAI1 BINDING SITE, designated SEQ ID:7841, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7699] Another function of VGAM61 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Alpha Inhibiting Activity Polypeptide 1 (GNAI1, Accession NM_002069), a gene which is involved as modulators or transducers in various transmembrane signaling systems. Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNAI1. The function of GNAI1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. General Transcription Factor IIF, Polypeptide 1, 74kDa (GTF2F1, Accession NM_002096) is another VGAM61 host target gene. GTF2F1 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by GTF2F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF2F1 BINDING SITE, designated SEQ ID:7885, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7700] Another function of VGAM61 is therefore inhibition of General Transcription Factor IIF, Polypeptide 1, 74kDa (GTF2F1, Accession NM_002096), a gene which helps to recruit it to the initiation complex in collaboration with tfiib. it promotes transcription elongation. Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF2F1. The function of GTF2F1 has been established by previous studies. At least 6 chromatographically resolvable general transcription factors may participate in accurate initiation by RNA polymerase II in HeLa cell-derived systems. TFIIF can bind directly to RNA polymerase II in solution and decrease the affinity of RNA polymerase II for nonspecific DNA. TFIIF is known to act at an intermediate stage in initiation complex formation. It

acts after TFIID (OMIM Ref. No. 313650) firmly associates with DNA, but coincidentally with or immediately after RNA polymerase II binding to DNA, and before the recruitment of factor TFIIIE (189962, 189964). The small subunit (RAP30; 189969) of TFIIF was cloned by Sopta et al. (1989) and shown to have some amino acid sequence homology to bacterial sigma factors. Aso et al. (1992) partially sequenced the RAP74 protein from purified HeLa cells, cloned its cDNA, and showed that its translation product can interact with RAP30 in vitro as well as in vivo. The cDNA predicted an amino acid sequence that lacks obvious DNA or RNA helicase motifs. Finkelstein et al. (1992) likewise isolated a cDNA encoding RAP74 and showed that both RAP30 and RAP74 produced in *Escherichia coli* could be used in place of natural human RAP30/74 to direct accurate transcription initiation by RNA polymerase II in vitro.

[7701] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7702] Sopta, M.; Burton, Z. F.; Greenblatt, J. : Structure and associated DNA-helicase activity of a general transcription initiation factor that binds to RNA polymerase II. *Nature*

341: 410–414, 1989. ; and

[7703] Finkelstein, A.; Kostrub, C. F.; Li, J.; Chavez, D. P.; Wang, B. Q.; Fang, S. M.; Greenblatt, J.; Burton, Z. F. : A cDNA encoding RAP74, a general initiation factor for transcription by.

[7704] Further studies establishing the function and utilities of GTF2F1 are found in John Hopkins OMIM database record ID 189968, and in cited publications numbered 9701–9705 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0527 (Accession XM_171054) is another VGAM61 host target gene. KIAA0527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0527 BINDING SITE, designated SEQ ID:45851, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7705] Another function of VGAM61 is therefore inhibition of KIAA0527 (Accession XM_171054). Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0527. Synaptophysin-like Protein (SYPL, Accession XM_167511) is another VGAM61 host target gene. SYPL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYPL BINDING SITE, designated SEQ ID:44644, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7706] Another function of VGAM61 is therefore inhibition of Synaptophysin-like Protein (SYPL, Accession XM_167511). Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYPL. LOC145820 (Accession XM_085246) is another VGAM61 host target gene. LOC145820 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145820 BINDING SITE, designated SEQ ID:37989, to

the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7707] Another function of VGAM61 is therefore inhibition of LOC145820 (Accession XM_085246). Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145820. LOC201627 (Accession XM_114353) is another VGAM61 host target gene. LOC201627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201627 BINDING SITE, designated SEQ ID:42898, to the nucleotide sequence of VGAM61 RNA, herein designated VGAM RNA, also designated SEQ ID:2772.

[7708] Another function of VGAM61 is therefore inhibition of LOC201627 (Accession XM_114353). Accordingly, utilities of VGAM61 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201627. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 62 (VGAM62) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7709] VGAM62 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM62 was detected is described hereinabove with reference to Figs. 1–8.

[7710] VGAM62 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7711] VGAM62 gene encodes a VGAM62 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM62 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM62 precursor RNA is designated SEQ ID:48, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:48 is located at position 134360 relative to the genome of Invertebrate Iridescent Virus 6.

[7712] VGAM62 precursor RNA folds onto itself, forming VGAM62 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7713] An enzyme complex designated DICER COMPLEX, `dices` the VGAM62 folded precursor RNA into VGAM62 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM62 RNA is designated SEQ ID:2773, and is provided hereinbelow with reference to the sequence listing part.

[7714] VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM62 host target RNA, herein designated VGAM HOST

TARGET RNA. VGAM62 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7715] VGAM62 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM62 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM62 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region,

this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7716] The complementary binding of VGAM62 RNA, herein designated VGAM RNA, to host target binding sites on VGAM62 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM62 host target RNA into VGAM62 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7717] It is appreciated that VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM62 host target genes. The mRNA of each one of this plurality of VGAM62 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM62 RNA, herein designated VGAM RNA, and which when bound by VGAM62 RNA causes inhibition of translation of respective one or more VGAM62 host target proteins.

[7718] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM62 gene, herein designated VGAM GENE, on one or more VGAM62 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7719] It is yet further appreciated that a function of VGAM62 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM62 correlate with, and may be deduced from, the identity of the host target genes which VGAM62 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

[7720] Nucleotide sequences of the VGAM62 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM62 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM62 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM62 are further described hereinbelow with reference to Table 1.

[7721] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM62 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM62 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7722] As mentioned hereinabove with reference to Fig. 1, a function of VGAM62 gene, herein designated VGAM is inhibition of expression of VGAM62 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM62 correlate with, and may be deduced from, the identity of the target genes which VGAM62 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7723] Eyes Absent Homolog 1 (Drosophila) (EYA1, Accession NM_000503) is a VGAM62 host target gene. EYA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EYA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EYA1 BINDING SITE, designated SEQ ID:6117, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7724] A function of VGAM62 is therefore inhibition of Eyes Absent Homolog 1 (Drosophila) (EYA1, Accession NM_000503). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EYA1. Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767) is another VGAM62 host target gene. LZTR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LZTR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTR1 BINDING SITE, designated SEQ ID:13633, to the

nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7725] Another function of VGAM62 is therefore inhibition of Leucine–zipper–like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTR1. ERAP140 (Accession XM_059748) is another VGAM62 host target gene. ERAP140 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ERAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERAP140 BINDING SITE, designated SEQ ID:37089, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7726] Another function of VGAM62 is therefore inhibition of ERAP140 (Accession XM_059748). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERAP140. KIAA1557 (Accession XM_028289) is another VGAM62 host target gene. KIAA1557 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA1557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1557 BINDING SITE, designated SEQ ID:30639, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7727] Another function of VGAM62 is therefore inhibition of KIAA1557 (Accession XM_028289). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1557. PR Domain Containing 10 (PRDM10, Accession NM_020228) is another VGAM62 host target gene. PRDM10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRDM10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM10 BINDING SITE, designated SEQ ID:21499, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7728] Another function of VGAM62 is therefore inhibition of PR Domain Containing 10 (PRDM10, Accession NM_020228). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM10. Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131) is another VGAM62 host target gene. SRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRF BINDING SITE, designated SEQ ID:9097, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7729] Another function of VGAM62 is therefore inhibition of Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRF. LOC148709 (Accession XM_086281) is another VGAM62 host target gene. LOC148709 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC148709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148709 BINDING SITE, designated SEQ ID:38580, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7730] Another function of VGAM62 is therefore inhibition of LOC148709 (Accession XM_086281). Accordingly, utilities of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148709. LOC164295 (Accession XM_092767) is another VGAM62 host target gene. LOC164295 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164295 BINDING SITE, designated SEQ ID:40143, to the nucleotide sequence of VGAM62 RNA, herein designated VGAM RNA, also designated SEQ ID:2773.

[7731] Another function of VGAM62 is therefore inhibition of LOC164295 (Accession XM_092767). Accordingly, utilities

of VGAM62 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164295. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 63 (VGAM63) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7732] VGAM63 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM63 was detected is described hereinabove with reference to Figs. 1–8.

[7733] VGAM63 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7734] VGAM63 gene encodes a VGAM63 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM63 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM63 precursor RNA is designated SEQ ID:49, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:49 is located at position 98449 relative to the genome of Invertebrate Iridescent Virus 6.

[7735] VGAM63 precursor RNA folds onto itself, forming VGAM63 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7736] An enzyme complex designated DICER COMPLEX, `dices` the VGAM63 folded precursor RNA into VGAM63 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM63 RNA is designated SEQ ID:2774, and is

provided hereinbelow with reference to the sequence listing part.

[7737] VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM63 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7738] VGAM63 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM63 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM63 RNA,

herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7739] The complementary binding of VGAM63 RNA, herein designated VGAM RNA, to host target binding sites on VGAM63 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM63 host target RNA into VGAM63 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7740] It is appreciated that VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM63 host target genes. The mRNA of each one of this plurality of VGAM63 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM63 RNA, herein designated VGAM

RNA, and which when bound by VGAM63 RNA causes inhibition of translation of respective one or more VGAM63 host target proteins.

[7741] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM63 gene, herein designated VGAM GENE, on one or more VGAM63 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7742] It is yet further appreciated that a function of VGAM63 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM63 include diagnosis, prevention and

treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM63 correlate with, and may be deduced from, the identity of the host target genes which VGAM63 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7743] Nucleotide sequences of the VGAM63 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM63 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM63 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM63 are further described hereinbelow with reference to Table 1.

[7744] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM63 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM63 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7745] As mentioned hereinabove with reference to Fig. 1, a function of VGAM63 gene, herein designated VGAM is inhibition of expression of VGAM63 target genes. It is ap-

preciated that specific functions, and accordingly utilities, of VGAM63 correlate with, and may be deduced from, the identity of the target genes which VGAM63 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7746] KIAA0061 (Accession XM_043094) is a VGAM63 host target gene. KIAA0061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0061 BINDING SITE, designated SEQ ID:33890, to the nucleotide sequence of VGAM63 RNA, herein designated VGAM RNA, also designated SEQ ID:2774.

[7747] A function of VGAM63 is therefore inhibition of KIAA0061 (Accession XM_043094). Accordingly, utilities of VGAM63 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0061. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 64 (VGAM64) viral gene, which modulates expression of re-

spective host target genes thereof, the function and utility of which host target genes is known in the art.

[7748] VGAM64 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM64 was detected is described hereinabove with reference to Figs. 1–8.

[7749] VGAM64 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7750] VGAM64 gene encodes a VGAM64 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM64 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM64 precursor RNA is designated SEQ ID:50, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:50 is located at position 146673 relative to the genome of Invertebrate Iridescent Virus 6.

[7751] VGAM64 precursor RNA folds onto itself, forming VGAM64 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7752] An enzyme complex designated DICER COMPLEX, `dices` the VGAM64 folded precursor RNA into VGAM64 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM64 RNA is designated SEQ ID:2775, and is provided hereinbelow with reference to the sequence listing part.

[7753] VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM64 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7754] VGAM64 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM64 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM64 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[7755] The complementary binding of VGAM64 RNA, herein designated VGAM RNA, to host target binding sites on VGAM64 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM64 host target RNA into VGAM64 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7756] It is appreciated that VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM64 host target genes. The mRNA of each one of this plurality of VGAM64 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM64 RNA, herein designated VGAM RNA, and which when bound by VGAM64 RNA causes inhibition of translation of respective one or more VGAM64 host target proteins.

[7757] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM64 gene, herein designated VGAM GENE, on one or

more VGAM64 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7758] It is yet further appreciated that a function of VGAM64 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM64 correlate with, and may be deduced from, the identity of the host target genes which VGAM64 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7759] Nucleotide sequences of the VGAM64 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM64 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM64 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM64 are further de-
scribed hereinbelow with reference to Table 1.

[7760] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM64 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM64 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[7761] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM64 gene, herein designated VGAM is in-
hibition of expression of VGAM64 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM64 correlate with, and may be deduced from, the
identity of the target genes which VGAM64 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[7762] Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774) is a
VGAM64 host target gene. ANK1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by ANK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE, designated SEQ ID:30284, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7763] A function of VGAM64 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933) is another VGAM64 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32511, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7764] Another function of VGAM64 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. BLAME (Accession NM_020125) is another VGAM64 host target gene. BLAME BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ ID:21306, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7765] Another function of VGAM64 is therefore inhibition of BLAME (Accession NM_020125). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. Caudal Type Homeo Box Transcription Factor 1 (CDX1, Accession NM_001804) is another VGAM64 host target gene. CDX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDX1, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDX1 BINDING SITE, designated SEQ ID:7557, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7766] Another function of VGAM64 is therefore inhibition of Caudal Type Homeo Box Transcription Factor 1 (CDX1, Accession NM_001804), a gene which could play a role in the terminal differentiation of the intestine. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDX1. The function of CDX1 has been established by previous studies. CDX1 is a member of the caudal-type homeo box family of genes. These are cognates of the *Drosophila* 'caudal' gene, which is required for anterior-posterior regional identity. Homologous genes have been found in mouse, rat, chicken, and *Xenopus*. CDX3 (OMIM Ref. No. 600297) is the human caudal-type homeo box gene located on chromosome 13. The caudal-type homeo box genes are members of the hexapeptide (HEX) super-class, containing a conserved hexapeptide motif upstream of the homeodomain, usually separated from the homeodomain by an intron. Bonner et al. (1995) isolated the

human CDX1 gene from a small intestine cDNA library using a murine Cdx1 cDNA probe. The nucleotide sequence of CDX1 was 81% identical to murine Cdx1 and predicted a 265-amino acid protein with 85% identity to the mouse protein (or 98% identity when the conservative amino acid changes were included). The murine Cdx1 gene maps to mouse chromosome 18, near Csfmr and Pdgfrb, in a region of conserved synteny with human 5q31-q33. Bonner et al. (1995) demonstrated that the human cognate of Cdx1 maps to a cosmid contig from 5q31-q33, placing CDX1 approximately 100 kb distal to CSF1R (OMIM Ref. No. 164770). (CSF1R had been mapped to 5q33.2-q33.3.) Northern analysis indicated that expression of CDX1 in adults appears to be limited to the intestine and colon, suggesting a possible role in the terminal differentiation of the intestine. In the mouse, Cdx1 is expressed along the embryonic axis from day 7.5 postcoitum until day 12, by which time the anterior limit of expression has regressed from the hindbrain level to the forelimb bud region. To assign a functional role for Cdx1 in murine embryonic development, Subramanian et al. (1995) inactivated the gene via homologous recombination. Viable fertile homozygous mutant mice were obtained that showed

anterior homeotic transformations of vertebrae. These abnormalities were concomitant with posterior shifts of Hox gene expression domains in the somitic mesoderm. The authors stated that the presence of putative Cdx1-binding sites in Hox gene control regions as well as in vitro trans-activation of Hoxa7 indicates a direct regulation.

[7767] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7768] Subramanian, V.; Meyer, B. I.; Gruss, P. : Disruption of the murine homeobox gene Cdx1 affects axial skeletal identities by altering the mesodermal expression domains of Hox genes. Cell 83: 641–653, 1995. ; and

[7769] Treacher Collins Syndrome Collaborative Group : Positional cloning of a gene involved in the pathogenesis of Treacher Collins syndrome. Nature Genet. 12: 130–136, 1996.

[7770] Further studies establishing the function and utilities of CDX1 are found in John Hopkins OMIM database record ID 600746, and in cited publications numbered 7584–758 and 3538 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Diacylglycerol O-acyltransferase Homolog 2 (mouse)

(DGAT2, Accession NM_032564) is another VGAM64 host target gene. DGAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DGAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGAT2 BINDING SITE, designated SEQ ID:26290, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7771] Another function of VGAM64 is therefore inhibition of Diacylglycerol O-acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM_032564). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGAT2. Fucosyltransferase 3 (galactoside 3(4)-L-fucosyltransferase, Lewis Blood Group Included) (FUT3, Accession NM_000149) is another VGAM64 host target gene. FUT3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FUT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FUT3 BINDING SITE, designated SEQ ID:5647, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7772] Another function of VGAM64 is therefore inhibition of Fucosyltransferase 3 (galactoside 3(4)-L-fucosyltransferase, Lewis Blood Group Included) (FUT3, Accession NM_000149), a gene which may catalyze alpha-1,3 and alpha-1,4 glycosidic linkages involved in the expression of vim-2, lewis a, lewis b, sialyl lewis x and lewis x/ssea-1 antigens. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT3. The function of FUT3 has been established by previous studies. The Lewis system involves genetically variable antigens in the body fluids and only secondarily are the antigens absorbed to red cells. Grollman et al. (1969) showed that Lewis-negative women lack a specific fucosyltransferase which is present in the milk of Lewis-positive women. The enzyme is apparently required for synthesis of the structural determinants of both Lewis (a) and Lewis (b) specificity. The same enzyme is involved in the synthesis of milk oligosaccharides, because 2 oligosaccharides containing the relevant

linkage were absent from the milk of Lewis-negative women. Grubb (1953) provided the ingenious interpretation of the interactions between the Les locus determining presence/absence of Lewis substance in the saliva and on red cells and the Se locus (OMIM Ref. No. 182100) determining secretion of ABH blood group substances in the saliva and Le(a) or Le(b) expression in red cells. In transfusion medicine, it has been found that some individuals who type as Lewis-positive on erythrocytes can change their erythrocyte phenotype to Lewis-negative during diseases or during pregnancy. Orntoft et al. (1996) noted that these patients have been named non-genuine Lewis-negative individuals as they have alpha-1-4 fucosyltransferase activity in saliva. Due to this phenomenon, the Lewis-negative phenotype is more common among cancer patients (approximately 20%) than among healthy individuals (approximately 8%). Orntoft et al. (1996) examined the mutational spectrum of the Lewis gene in Denmark and found 6 different mutations. Five, 59T-G (L20R; 111100.0001), 202T-C (W68R), 314C-T (T105M), 508G-A (G170S; 111100.0001), and 1067T-A (I356K), were frequent, and 1, 445C-A (L146M), was only detected in 1 of 40 individuals. The authors demonstrated that the nu-

cleotide 202 and 314 mutations were located on the same allele. COS-7 cells transfected with an allele having the 202/314 mutations lacked enzyme activity. Lewis-negative patients, whose erythrocytes converted from Lewis-positive to Lewis-negative during their disease, showed FUT3 heterozygosity significantly more often than did others (p less than 0.05). Pang et al. (1998) identified 5 novel missense mutations in the FUT3 gene in African (Xhosa) and Caucasian subjects in South Africa.

[7773] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7774] Grollman, E. F.; Kobata, A.; Ginsburg, V. : An enzymatic basis for Lewis blood types in man. J. Clin. Invest. 48: 1489-1494, 1969. ; and

[7775] Orntoft, T. F.; Vestergaard, E. M.; Holmes, E.; Jakobsen, J. S.; Grunnet, N.; Mortensen, M.; Johnson, P.; Bross, P.; Gregersen, N.; Skorstengaard, K.; Jensen, U. B.; Bolund, L.; Wolf, H.

[7776] Further studies establishing the function and utilities of FUT3 are found in John Hopkins OMIM database record ID 111100, and in cited publications numbered 10702, 10703-24 and 3780-244 listed in the bibliography sec-

tion hereinbelow, which are also hereby incorporated by reference. Fucosyltransferase 8 (alpha (1,6) Fucosyltransferase) (FUT8, Accession NM_004480) is another VGAM64 host target gene. FUT8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT8 BINDING SITE, designated SEQ ID:10796, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7777] Another function of VGAM64 is therefore inhibition of Fucosyltransferase 8 (alpha (1,6) Fucosyltransferase) (FUT8, Accession NM_004480), a gene which transfers fucose to N-linked type complex glycopeptides from GDP-Fuc; functions in asparagine-linked glycoprotein oligosaccharide synthesis. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT8. The function of FUT8 has been established by previous studies. Alpha-1,6-fucosyltransferase catalyzes the transfer of fucose to N-linked glycopeptides. Yanagidani et al. (1997) purified a

60-kD alpha-1,6-fucosyltransferase from a human gastric cancer cell line and used peptide sequences to clone the FUT8 cDNA. The gene encodes a 575-amino acid polypeptide that has little sequence homology to other human fucosyltransferases. Costache et al. (1997) analyzed FUT sequences in the GenBank expressed sequence tag (EST) database and noted that FUT8 is represented more frequently, possibly indicating that it has a higher level of expression than other FUT genes. They also identified a slightly longer alternatively spliced variant of FUT8 from retina cDNA libraries. Costache et al. (1997) reviewed the evolutionary relationships among known fucosyltransferase genes. The phylogenetic branch point for FUT8 was the oldest.

[7778] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7779] Costache, M.; Apoil, P.-A.; Cailleau, A.; Elmgren, A.; Larson, G.; Henry, S.; Blancher, A.; Iordachescu, D.; Oriol, R.; Mollicone, R. : Evolution of fucosyltransferase genes in vertebrates. *J. Biol. Chem.* 272: 29721–29728, 1997. ; and

[7780] Yanagidani, S.; Uozumi, N.; Ihara, Y.; Miyoshi, E.; Yamaguchi, N.; Taniguchi, N. : Purification and cDNA cloning

of GDP-L-Fuc:N-acetyl-beta-D-glucosaminide:alpha-1-6 fucosyltransferase.

[7781] Further studies establishing the function and utilities of FUT8 are found in John Hopkins OMIM database record ID 602589, and in cited publications numbered 8635-8636 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Gap Junction Protein, Alpha 5, 40kDa (connexin 40) (GJA5, Accession XM_059147) is another VGAM64 host target gene. GJA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GJA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GJA5 BINDING SITE, designated SEQ ID:36902, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7782] Another function of VGAM64 is therefore inhibition of Gap Junction Protein, Alpha 5, 40kDa (connexin 40) (GJA5, Accession XM_059147), a gene which may facilitate cardiac impulse conduction. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GJA5. The function of

GJA5 has been established by previous studies. See 121011 for a general discussion of the connexin gene family. Kanter et al. (1992) demonstrated that canine ventricular myocytes express 3 distinct gap junction proteins, Cx40, Cx43 (GJA1; 121013), and Cx45. Kanter et al. (1994) used PCR with primers based on rat and dog Cx40 to clone human CX40. The CX40 gene has a 5-prime untranslated exon and 1 coding exon, and encodes a predicted 358-amino acid protein whose sequence is 82% identical to that of the rat and mouse CX40 protein. Northern blot analysis showed that CX40 mRNA is expressed as an approximately 3.3-kb transcript in ventricular myocardium. In immunofluorescence studies, CX40 localized to intercalated disc regions of the left ventricle, which join cardiac myocytes and contain gap junctions. The migration of lymphocytes from the circulation into tissues involves a number of adhesion molecules and the expression of new molecules. Gap junctions facilitate cell-to-cell adhesion and provide pathways for direct intercellular communication. Oviedo-Orta et al. (2000) noted that GJA1 is expressed in a number of lymphoid organs. By RT-PCR, Western blot, and flow cytometric analyses, they showed that lymphocytes express GJA1 and GJA5, but not

GJB2 (OMIM Ref. No. 121011), GJB1 (OMIM Ref. No. 304040), GJA4 (OMIM Ref. No. 121012), or GJA7; GJA5 expression was restricted to tonsillar T and B lymphocytes. Flow cytometric analysis showed that GJA1 and GJA5 expression increases after mitogenic stimulation. Extracellular connexin mimetic peptide blocked dye transfer between lymphocyte subpopulations, and gap junction inhibitors decreased the production of IgM in cocultured T and B lymphocytes. The results identified gap junction proteins as important cell surface components that modulate immune responses.

[7783] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7784] Kanter, H. L.; Saffitz, J. E.; Beyer, E. C. : Cardiac myocytes express multiple gap junction proteins. *Circ. Res.* 70: 438–444, 1992. ; and

[7785] Oviedo–Orta, E.; Hoy, T.; Evans, W. H. : Intercellular communication in the immune system: differential expression of connexin40 and 43, and perturbation of gap junction channel function.

[7786] Further studies establishing the function and utilities of GJA5 are found in John Hopkins OMIM database record ID

121013, and in cited publications numbered 11840–1184 and 11839 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Inositol Polyphosphate–5–phosphatase, 145kDa (INPP5D, Accession XM_096169) is another VGAM64 host target gene. INPP5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INPP5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INPP5D BINDING SITE, designated SEQ ID:40306, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7787] Another function of VGAM64 is therefore inhibition of Inositol Polyphosphate–5–phosphatase, 145kDa (INPP5D, Accession XM_096169), a gene which hydrolyzes Ins(1,3,4,5)P₄ and PtdIns(3,4,5)P₃; contains an SH2–domain. Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INPP5D. The function of INPP5D has been established by previous studies. The phosphatidylinositols serve as precursors for a number of

different messenger molecules. Agonist stimulation of cells results in phosphatidylinositol turnover and the generation of inositol 1,4,5-triphosphate (Ins(1,4,5)P₃), which mobilizes intracellular calcium. The inositol-polyphosphate 5-phosphatase (INPP5) enzymes hydrolyze Ins(1,4,5)P₃ in a signal-terminating reaction. Known INPP5s include the 40-kD INPP5A (OMIM Ref. No. 600106), the 75-kD INPP5B (OMIM Ref. No. 147264), and the enzyme associated with Lowe oculocerebrorenal syndrome (OMIM Ref. No. 309000). Damen et al. (1996) cloned and sequenced a cDNA encoding a 145-kD protein from a mouse hematopoietic cell line; the protein became tyrosine phosphorylated and associated with SHC (OMIM Ref. No. 600560) after cytokine stimulation. Based on its domains and enzymatic activity, Damen et al. (1996) named this protein SHIP for 'SH2-containing inositol phosphatase. Liu et al. (1998) studied the expression of the Ship gene during mouse development. They found that the gene is expressed in late primitive-streak stage embryos (7.5 days post coitum), when hematopoiesis is thought to begin, and the expression is restricted to the hematopoietic lineage. In adult mice, Ship expression continues in most cells of hematopoietic origin, including

granulocytes, monocytes, and lymphocytes, and is also found in the spermatids of the testis. Furthermore, the level of Ship expression is developmentally regulated during T-cell maturation. These results suggested a possible role for Ship in the differentiation and maintenance of the hematopoietic lineages and in spermatogenesis. Animal model experiments lend further support to the function of INPP5D. Because Ship $-/-$ mice contain increased numbers of osteoclast precursors, i.e., macrophages, Takeshita et al. (2002) examined bones from these animals and found that osteoclast number was increased 2-fold. The increased number was the result of prolonged lifespan of these cells and hypersensitivity of precursors to macrophage colony-stimulating factor (M-CSF; 120420) and receptor activator of nuclear factor- κ B ligand (RANKL; 602642). Similar to the osteoclasts of Paget disease of bone (OMIM Ref. No. 602080), Ship $-/-$ osteoclasts were enlarged, containing upwards of 100 nuclei, and exhibited enhanced resorptive activity. Moreover, as in Paget disease, serum levels of interleukin-6 (OMIM Ref. No. 147620) were markedly increased in Ship $-/-$ mice. Consistent with accelerated resorptive activity, a 22% loss of bone-mineral density and a 49% decrease in fracture

energy were observed. Thus, SHIP negatively regulates osteoclast formation and function, and the absence of this enzyme results in severe osteoporosis

[7788] It is appreciated that the abovementioned animal model for INPP5D is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7789] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7790] Liu, Q.; Shalaby, F.; Jones, J.; Bouchard, D.; Dumont, D. J. : The SH2-containing inositol polyphosphate 5-phosphatase, Ship, is expressed during hematopoiesis and spermatogenesis. Blood 91: 2753–2759, 1998. ; and

[7791] Takeshita, S.; Namba, N.; Zhao, J. J.; Jiang, Y.; Genant, H. K.; Silva, M. J.; Brodt, M. D.; Helgason, C. D.; Kalesnikoff, J.; Rauh, M. J.; Humphries, R. K.; Krystal, G.; Teitelbaum, S.

[7792] Further studies establishing the function and utilities of INPP5D are found in John Hopkins OMIM database record ID 601582, and in cited publications numbered 6540–6550 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphorylase, Glycogen; Brain (PYGB, Accession

NM_002862) is another VGAM64 host target gene. PYGB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PYGB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PYGB BINDING SITE, designated SEQ ID:8768, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7793] Another function of VGAM64 is therefore inhibition of Phosphorylase, Glycogen; Brain (PYGB, Accession NM_002862). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PYGB. Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM_130845) is another VGAM64 host target gene. SNTB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNTB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTB2 BINDING SITE, designated SEQ ID:28378, to the nucleotide sequence of

VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7794] Another function of VGAM64 is therefore inhibition of Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM_130845). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTB2. Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM_000362) is another VGAM64 host target gene. TIMP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMP3 BINDING SITE, designated SEQ ID:5933, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7795] Another function of VGAM64 is therefore inhibition of Tissue Inhibitor of Metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3, Accession NM_000362). Accordingly, utilities of VGAM64 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with TIMP3. Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession NM_003938) is another VGAM64 host target gene. AP3D1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AP3D1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3D1 BINDING SITE, designated SEQ ID:10049, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7796] Another function of VGAM64 is therefore inhibition of Adaptor-related Protein Complex 3, Delta 1 Subunit (AP3D1, Accession NM_003938). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3D1. Bromodomain Containing 2 (BRD2, Accession NM_005104) is another VGAM64 host target gene. BRD2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BRD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of BRD2 BINDING SITE, designated SEQ ID:11574, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7797] Another function of VGAM64 is therefore inhibition of Bromodomain Containing 2 (BRD2, Accession NM_005104). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD2. Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575) is another VGAM64 host target gene. C17orf31 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:19001, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7798] Another function of VGAM64 is therefore inhibition of Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with C17orf31. CG018 (Accession NM_052818) is another VGAM64 host target gene. CG018 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CG018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG018 BINDING SITE, designated SEQ ID:27403, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7799] Another function of VGAM64 is therefore inhibition of CG018 (Accession NM_052818). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG018. DKFZp434F142 (Accession NM_032254) is another VGAM64 host target gene. DKFZp434F142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F142 BINDING SITE, designated SEQ ID:25994, to

the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7800] Another function of VGAM64 is therefore inhibition of DKFZp434F142 (Accession NM_032254). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F142. DnaJ (Hsp40) Homolog, Subfamily C, Member 5 (DNAJC5, Accession XM_028966) is another VGAM64 host target gene. DNAJC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJC5 BINDING SITE, designated SEQ ID:30812, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7801] Another function of VGAM64 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily C, Member 5 (DNAJC5, Accession XM_028966). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJC5. FLJ11506 (Accession NM_024666) is another VGAM64 host target

gene. FLJ11506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11506 BINDING SITE, designated SEQ ID:23967, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7802] Another function of VGAM64 is therefore inhibition of FLJ11506 (Accession NM_024666). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11506. FLJ12190 (Accession NM_025071) is another VGAM64 host target gene. FLJ12190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12190 BINDING SITE, designated SEQ ID:24667, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7803] Another function of VGAM64 is therefore inhibition of FLJ12190 (Accession NM_025071). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12190. FLJ14816 (Accession NM_032845) is another VGAM64 host target gene. FLJ14816 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14816, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14816 BINDING SITE, designated SEQ ID:26638, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7804] Another function of VGAM64 is therefore inhibition of FLJ14816 (Accession NM_032845). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14816. Interleukin 14 (IL14, Accession XM_170924) is another VGAM64 host target gene. IL14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL14 BINDING SITE, designated SEQ ID:45704, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7805] Another function of VGAM64 is therefore inhibition of Interleukin 14 (IL14, Accession XM_170924). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL14. KIAA0265 (Accession XM_045954) is another VGAM64 host target gene. KIAA0265 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0265 BINDING SITE, designated SEQ ID:34628, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7806] Another function of VGAM64 is therefore inhibition of KIAA0265 (Accession XM_045954). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0265. KIAA0495 (Accession XM_031397) is another VGAM64 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31363, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7807] Another function of VGAM64 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA1045 (Accession XM_048592) is another VGAM64 host target gene. KIAA1045 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35200, to the nucleotide sequence of VGAM64 RNA, herein designated

VGAM RNA, also designated SEQ ID:2775.

[7808] Another function of VGAM64 is therefore inhibition of KIAA1045 (Accession XM_048592). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1045. KIAA1529 (Accession XM_047336) is another VGAM64 host target gene. KIAA1529 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1529 BINDING SITE, designated SEQ ID:34948, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7809] Another function of VGAM64 is therefore inhibition of KIAA1529 (Accession XM_047336). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1529. KIAA1719 (Accession XM_042936) is another VGAM64 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1719, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33819, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7810] Another function of VGAM64 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. LRG (Accession NM_052972) is another VGAM64 host target gene. LRG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRG BINDING SITE, designated SEQ ID:27547, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7811] Another function of VGAM64 is therefore inhibition of LRG (Accession NM_052972). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with LRG. MGC23980 (Accession NM_145005) is another VGAM64 host target gene. MGC23980 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC23980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC23980 BINDING SITE, designated SEQ ID:29607, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7812] Another function of VGAM64 is therefore inhibition of MGC23980 (Accession NM_145005). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC23980. Mitochondrial Ribosomal Protein S10 (MRPS10, Accession NM_018141) is another VGAM64 host target gene. MRPS10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPS10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPS10 BINDING SITE,

designated SEQ ID:19939, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7813] Another function of VGAM64 is therefore inhibition of Mitochondrial Ribosomal Protein S10 (MRPS10, Accession NM_018141). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPS10. Nei Like 2 (E. coli) (NEIL2, Accession NM_145043) is another VGAM64 host target gene. NEIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEIL2 BINDING SITE, designated SEQ ID:29673, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7814] Another function of VGAM64 is therefore inhibition of Nei Like 2 (E. coli) (NEIL2, Accession NM_145043). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEIL2. Protein Kinase C and Casein Kinase Sub-

strate In Neurons 2 (PACSIN2, Accession NM_007229) is another VGAM64 host target gene. PACSIN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PACSIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACSIN2 BINDING SITE, designated SEQ ID:14096, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7815] Another function of VGAM64 is therefore inhibition of Protein Kinase C and Casein Kinase Substrate In Neurons 2 (PACSIN2, Accession NM_007229). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACSIN2. PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975) is another VGAM64 host target gene. PTK6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PTK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK6 BINDING SITE, designated SEQ ID:12599, to the nu-

cleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7816] Another function of VGAM64 is therefore inhibition of PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK6. TAO1 (Accession NM_004783) is another VGAM64 host target gene. TAO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAO1 BINDING SITE, designated SEQ ID:11190, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7817] Another function of VGAM64 is therefore inhibition of TAO1 (Accession NM_004783). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAO1. LOC123591 (Accession XM_063741) is another VGAM64 host target gene. LOC123591 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by LOC123591, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123591 BINDING SITE, designated SEQ ID:37251, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7818] Another function of VGAM64 is therefore inhibition of LOC123591 (Accession XM_063741). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123591. LOC143286 (Accession XM_096412) is another VGAM64 host target gene. LOC143286 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143286, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143286 BINDING SITE, designated SEQ ID:40356, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7819] Another function of VGAM64 is therefore inhibition of LOC143286 (Accession XM_096412). Accordingly, utilities

of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143286. LOC150271 (Accession XM_097859) is another VGAM64 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41175, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7820] Another function of VGAM64 is therefore inhibition of LOC150271 (Accession XM_097859). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC151176 (Accession XM_098016) is another VGAM64 host target gene. LOC151176 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC151176 BINDING SITE, designated SEQ ID:41315, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7821] Another function of VGAM64 is therefore inhibition of LOC151176 (Accession XM_098016). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151176. LOC196478 (Accession XM_113729) is another VGAM64 host target gene. LOC196478 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196478 BINDING SITE, designated SEQ ID:42379, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7822] Another function of VGAM64 is therefore inhibition of LOC196478 (Accession XM_113729). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196478. LOC254268 (Accession XM_170913) is another VGAM64 host target gene. LOC254268 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254268 BINDING SITE, designated SEQ ID:45692, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7823] Another function of VGAM64 is therefore inhibition of LOC254268 (Accession XM_170913). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254268. LOC56912 (Accession NM_020153) is another VGAM64 host target gene. LOC56912 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56912 BINDING SITE, designated SEQ ID:21364, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7824] Another function of VGAM64 is therefore inhibition of

LOC56912 (Accession NM_020153). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56912. LOC92710 (Accession XM_046811) is another VGAM64 host target gene. LOC92710 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92710, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92710 BINDING SITE, designated SEQ ID:34834, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7825] Another function of VGAM64 is therefore inhibition of LOC92710 (Accession XM_046811). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92710. LOC93190 (Accession XM_049705) is another VGAM64 host target gene. LOC93190 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC93190 BINDING SITE, designated SEQ ID:35488, to the nucleotide sequence of VGAM64 RNA, herein designated VGAM RNA, also designated SEQ ID:2775.

[7826] Another function of VGAM64 is therefore inhibition of LOC93190 (Accession XM_049705). Accordingly, utilities of VGAM64 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93190. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 65 (VGAM65) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7827] VGAM65 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM65 was detected is described hereinabove with reference to Figs. 1–8.

[7828] VGAM65 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[7829] VGAM65 gene encodes a VGAM65 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM65 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM65 precursor RNA is designated SEQ ID:51, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:51 is located at position 84924 relative to the genome of Invertebrate Iridescent Virus 6.

[7830] VGAM65 precursor RNA folds onto itself, forming VGAM65 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7831] An enzyme complex designated DICER COMPLEX, `dices` the VGAM65 folded precursor RNA into VGAM65 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM65 RNA is designated SEQ ID:2776, and is provided hereinbelow with reference to the sequence listing part.

[7832] VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM65 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7833] VGAM65 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM65 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of

each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM65 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7834] The complementary binding of VGAM65 RNA, herein designated VGAM RNA, to host target binding sites on VGAM65 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM65 host target RNA into VGAM65 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7835] It is appreciated that VGAM65 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM65 host target genes. The mRNA of each one of this plurality of VGAM65 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM65 RNA, herein designated VGAM RNA, and which when bound by VGAM65 RNA causes inhibition of translation of respective one or more VGAM65 host target proteins.

[7836] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM65 gene, herein designated VGAM GENE, on one or more VGAM65 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7837] It is yet further appreciated that a function of VGAM65 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM65 correlate with, and may be deduced from, the identity of the host target genes which VGAM65 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7838] Nucleotide sequences of the VGAM65 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM65 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM65 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM65 are further described hereinbelow with reference to Table 1.

[7839] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM65 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM65 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7840] As mentioned hereinabove with reference to Fig. 1, a function of VGAM65 gene, herein designated VGAM is inhibition of expression of VGAM65 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM65 correlate with, and may be deduced from, the identity of the target genes which VGAM65 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7841] UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Accession NM_014256) is a VGAM65 host target gene. B3GNT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B3GNT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT3 BINDING SITE, designated SEQ ID:15534, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7842] A function of VGAM65 is therefore inhibition of UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Accession NM_014256). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT3. 5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870) is another VGAM65 host target gene. HTR4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR4 BINDING SITE, designated SEQ ID:6546, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7843] Another function of VGAM65 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870), a gene which mediates calcium channel currents. Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR4. The function of HTR4 has been established by previous studies. The

5-hydroxytryptamine-4 receptor was first characterized by Dumuis et al. (1988) in mouse colliculi neurons. Subsequently, Eglen et al. (1995) showed that 5-HT₄ mediates widespread effects in central and peripheral nervous systems. Serotonin acts as a stimulant to atrial cardiac cells in only a few mammalian species including human, monkey, and pig but not rodents. Cells from human atrium respond to 5-HT stimulation by producing an L-type calcium current. Blondel et al. (1997) used PCR, based on primers to the central region of rat 5-HT₄ receptor, to clone a human 5-HT₄ receptor, which they called 5-HT_{4A}. Sequence analysis showed that this cDNA encodes a 387-amino acid polypeptide with 7 putative transmembrane domains and several potential regulatory sites. Blondel et al. (1997) found that 5-HT_{4A} is the same length and 93% identical to the shorter of the 2 alternately spliced forms of the rat 5-HT₄ receptor. RT-PCR analysis showed that the 5-HT_{4A} mRNA is expressed in human ileum, brain, and atrium, but not in the ventricle. COS-7 cells expressing the 5-HT₄ receptor respond to serotonin stimulation with pharmacologic profiles similar to those seen in human atrial myocytes, suggesting to Blondel et al. (1997) that 5-HT_{4A} is the protein responsible for the

serotonin responsiveness of the human atrium.

- [7844] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [7845] Claeyssen, S.; Faye, P.; Sebben, M.; Lemaire, S.; Bockaert, J.; Dumuis, A.; Taviaux, S. : Assignment of 5-hydroxytryptamine receptor (HTR4) to human chromosome 5 bands q31-to-q33 by in situ hybridization. *Cytogenet. Cell Genet.* 78: 133-134, 1997. ; and
- [7846] Dumuis, A.; Bouhelal, R.; Sebben, M.; Cory, R.; Bockaert, J. : A nonclassical 5-hydroxytryptamine receptor positively coupled with adenylate cyclase in the central nervous system. *Molec.*
- [7847] Further studies establishing the function and utilities of HTR4 are found in John Hopkins OMIM database record ID 602164, and in cited publications numbered 6342-6345 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PSA (Accession NM_021154) is another VGAM65 host target gene. PSA BINDING SITE1 and PSA BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PSA, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSA BINDING SITE1 and PSA BINDING SITE2, designated SEQ ID:22129 and SEQ ID:27738 respectively, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7848] Another function of VGAM65 is therefore inhibition of PSA (Accession NM_021154), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSA. The function of PSA has been established by previous studies. Tobler et al. (1997) cloned PSA from a human fetal brain cDNA library using the mouse PSA cDNA as probe. They established that translation is initiated at the second of 2 possible start codons, resulting in a deduced 875-amino acid protein with a molecular mass of 99 kD by SDS-PAGE. PSA contains a zinc-binding motif conserved among gluzincin aminopeptidases and shares 98% sequence identity with the mouse protein. Northern blot analysis detected ubiquitous expression of a 4.8-kb transcript, with highest expression in brain. By in situ hybridization of adult human brain sections, expres-

sion was localized to the perikaryon of neurons of the cortex and cerebellum. Using immunofluorescence localization of transfected HeLa cells, Tobler et al. (1997) found that PSA localizes to the perinuclear cytoplasm and shows a filamentous staining pattern. Bauer et al. (2001) cloned PSA cDNA from a human skeletal muscle library. Northern blot analysis detected major and minor transcripts of 4.8 and 4.2 kb, respectively. Huber et al. (1999) determined that PSA is identical to the metalloprotease MP100 that was originally isolated as a beta-secretase candidate from human brain by Schonlein et al. (1994). Huber et al. (1999) were able to colocalize and coimmunoprecipitate PSA with beta-amyloid precursor protein (OMIM Ref. No. 104760); however, PSA did not increase production of the amyloid-beta peptide in cotransfected cells. By RT-PCR, but not by Northern blot analysis, Bauer et al. (2001) found that PSA was upregulated in human leukemic cells following vitamin D stimulation.

[7849] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7850] Huber, G.; Thompson, A.; Gruninger, F.; Mechler, H.; Hochstrasser, R.; Hauri, H.-P.; Malherbe, P. : cDNA cloning

and molecular characterization of human brain metallo-protease MP100: a beta-secretase candidate? J. Neurochem. 72: 1215-1223, 1999. ; and

[7851] Tobler, A. R.; Constam, D. B.; Schmitt-Graff, A.; Malipiero, U.; Schlapbach, R.; Fontana, A. : Cloning of the human puromycin-sensitive aminopeptidase and evidence for expression in neu.

[7852] Further studies establishing the function and utilities of PSA are found in John Hopkins OMIM database record ID 606793, and in cited publications numbered 5485-5490 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp761B0514 (Accession NM_032289) is another VGAM65 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26052, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7853] Another function of VGAM65 is therefore inhibition of DK-

FZp761B0514 (Accession NM_032289). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B0514. FLJ10290 (Accession NM_018047) is another VGAM65 host target gene. FLJ10290 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10290 BINDING SITE, designated SEQ ID:19798, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7854] Another function of VGAM65 is therefore inhibition of FLJ10290 (Accession NM_018047). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10290. KIAA1841 (Accession XM_087056) is another VGAM65 host target gene. KIAA1841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA1841 BINDING SITE, designated SEQ ID:39028, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7855] Another function of VGAM65 is therefore inhibition of KIAA1841 (Accession XM_087056). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1841. UQCR (Accession NM_006830) is another VGAM65 host target gene. UQCR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UQCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UQCR BINDING SITE, designated SEQ ID:13710, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7856] Another function of VGAM65 is therefore inhibition of UQCR (Accession NM_006830). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UQCR. Zinc Finger, Imprinted 3 (ZIM3, Accession NM_052882) is

another VGAM65 host target gene. ZIM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZIM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZIM3 BINDING SITE, designated SEQ ID:27462, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7857] Another function of VGAM65 is therefore inhibition of Zinc Finger, Imprinted 3 (ZIM3, Accession NM_052882). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZIM3. LOC113523 (Accession XM_054378) is another VGAM65 host target gene. LOC113523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113523 BINDING SITE, designated SEQ ID:36156, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7858] Another function of VGAM65 is therefore inhibition of LOC113523 (Accession XM_054378). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113523. LOC143465 (Accession XM_096430) is another VGAM65 host target gene. LOC143465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143465 BINDING SITE, designated SEQ ID:40366, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7859] Another function of VGAM65 is therefore inhibition of LOC143465 (Accession XM_096430). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143465. LOC92539 (Accession XM_045632) is another VGAM65 host target gene. LOC92539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92539, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92539 BINDING SITE, designated SEQ ID:34505, to the nucleotide sequence of VGAM65 RNA, herein designated VGAM RNA, also designated SEQ ID:2776.

[7860] Another function of VGAM65 is therefore inhibition of LOC92539 (Accession XM_045632). Accordingly, utilities of VGAM65 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92539. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 66 (VGAM66) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7861] VGAM66 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM66 was detected is described hereinabove with reference to Figs. 1–8.

[7862] VGAM66 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM66 host target gene, herein designated

VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7863] VGAM66 gene encodes a VGAM66 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM66 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM66 precursor RNA is designated SEQ ID:52, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:52 is located at position 112517 relative to the genome of Invertebrate Iridescent Virus 6.

[7864] VGAM66 precursor RNA folds onto itself, forming VGAM66 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7865] An enzyme complex designated DICER COMPLEX, `dices` the VGAM66 folded precursor RNA into VGAM66 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM66 RNA is designated SEQ ID:2777, and is provided hereinbelow with reference to the sequence listing part.

[7866] VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM66 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7867] VGAM66 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM66 RNA is an accurate or a partial in-

versed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM66 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7868] The complementary binding of VGAM66 RNA, herein designated VGAM RNA, to host target binding sites on VGAM66 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM66 host target RNA into VGAM66 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7869] It is appreciated that VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM66 host target genes. The mRNA of each one of this plurality of VGAM66 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM66 RNA, herein designated VGAM RNA, and which when bound by VGAM66 RNA causes inhibition of translation of respective one or more VGAM66 host target proteins.

[7870] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM66 gene, herein designated VGAM GENE, on one or more VGAM66 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although spe-

cific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7871] It is yet further appreciated that a function of VGAM66 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM66 correlate with, and may be deduced from, the identity of the host target genes which VGAM66 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7872] Nucleotide sequences of the VGAM66 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM66 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM66 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM66 are further described hereinbelow with reference to Table 1.

[7873] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM66 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM66 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7874] As mentioned hereinabove with reference to Fig. 1, a function of VGAM66 gene, herein designated VGAM is inhibition of expression of VGAM66 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM66 correlate with, and may be deduced from, the identity of the target genes which VGAM66 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7875] Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM_002074) is a VGAM66 host target gene. GNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB1 BINDING SITE, designated SEQ ID:7852, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7876] A function of VGAM66 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 1 (GNB1, Accession NM_002074). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB1.

Lecithin Retinol Acyltransferase

(phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM_011181) is another VGAM66 host target gene. LRAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRAT BINDING SITE, designated SEQ ID:30184, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7877] Another function of VGAM66 is therefore inhibition of Lecithin Retinol Acyltransferase (phosphatidylcholine--retinol O-acyltransferase) (LRAT, Accession XM_011181). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRAT. Retinal Pigment Epithelium-specific Protein 65kDa (RPE65, Accession

NM_000329) is another VGAM66 host target gene. RPE65 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPE65, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPE65 BINDING SITE, designated SEQ ID:5871, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7878] Another function of VGAM66 is therefore inhibition of Retinal Pigment Epithelium-specific Protein 65kDa (RPE65, Accession NM_000329), a gene which May play a role in vitamin-A metabolism of the retina. Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPE65. The function of RPE65 has been established by previous studies. The retinal pigment epithelium (RPE) is a monolayer simple epithelium apposed to the outer surface of the retinal photoreceptor cells. It is involved in many aspects of outer retinal metabolism that are essential to the continued maintenance of the photoreceptor cells, including many RPE-specific functions such as the retinoid visual cycle and photoreceptor outer segment disk phago-

cytosis and recycling. Hamel et al. (1993) characterized and cloned a unique RPE-specific microsomal protein, RPE65, that is conserved in vertebrates and was a candidate for the site of mutation in hereditary retinal disorders implicating the RPE. Using a human/hamster hybrid panel, Hamel et al. (1994) mapped the human RPE65 gene to chromosome 1 and, by fluorescence in situ hybridization, refined the localization to 1p31. Using interspecific back-cross analysis, they mapped the mouse Rpe65 gene to the distal portion of chromosome 3. Animal model experiments lend further support to the function of RPE65. Aguirre et al. (1998) described a 4-bp deletion in the RPE65 gene in a form of retinal dystrophy in dogs of the Swedish Briard breed. The disorder was initially described by Narfstrom et al. (1989) as a stationary disorder analogous to human congenital stationary night blindness (CSNB). The disorder was later described as having a progressive component and was termed hereditary retinal dystrophy (Wrigstad et al., 1994). Aguirre et al. (1998) studied 10 Briard dogs affected with what has been called CSNB in the U.S. The dogs originated from stock in the U.S., Canada, and France. Identification of the same mutation (a homozygous 4-bp deletion resulting in frameshift

and a premature stop codon that truncates the protein)
suggested a founder effect

[7879] It is appreciated that the abovementioned animal model for RPE65 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[7880] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7881] Hamel, C. P.; Jenkins, N. A.; Gilbert, D. J.; Copeland, N. G.; Redmond, T. M. : The gene for the retinal pigment epithelium-specific protein RPE65 is localized to human 1p31 and mouse 3. Genomics 20: 509–512, 1994. ; and

[7882] Aguirre, G. D.; Baldwin, V.; Pearce-Kelling, S.; Narfstrom, K.; Ray, K.; Acland, G. M. : Congenital stationary night blindness in the dog: common mutation in the RPE65 gene indicates found.

[7883] Further studies establishing the function and utilities of RPE65 are found in John Hopkins OMIM database record ID 180069, and in cited publications numbered 10465–1047 and 10072–10076 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 4, Sodium Bicarbonate

Cotransporter, Member 7 (SLC4A7, Accession NM_003615) is another VGAM66 host target gene. SLC4A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC4A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A7 BINDING SITE, designated SEQ ID:9674, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7884] Another function of VGAM66 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 7 (SLC4A7, Accession NM_003615), a gene which mediates the coupled movement of sodium and bicarbonate ions across the plasma membrane. Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A7. The function of SLC4A7 has been established by previous studies. By searching an EST database for sequences related to the pNBC variant of NBC1 (OMIM Ref. No. SLC4A4), Pushkin et al. (1999) identified ESTs encoding SLC4A7, which they called NBC3. They isolated human

muscle cDNAs representing a full-length NBC3 coding sequence. The predicted 1,214-amino acid muscle NBC3 variant, which the authors referred to as mNBC3, contains 12 putative transmembrane domains, with cytoplasmic N and C termini. mNBC3 has 1 putative stilbene-binding motif, numerous potential intracellular phosphorylation sites, potential sites for myristylation and amidation, and potential N-linked glycosylation sites in the exofacial loops between transmembrane domains 1 and 2, and 5 and 6. mNBC3 shares 78% amino acid sequence homology with the NBC2 variant (Ishibashi et al., 1998) of SLC4A7, 46% homology with the kNBC variant of NBC1, 39% homology with the pNBC variant of NBC1, and 29% homology with AE3 (SLC4A3; 106195). Expression of mNBC3 in *Xenopus* oocytes demonstrated that it is a stilbene-insensitive 5-(N-ethyl-N-isopropyl)-amiloride (EIPA)-inhibitable NBC. The SLC4A7 gene spans approximately 80 kb and contains 25 exons. Northern blot analysis of a number of human tissues detected an approximately 7.8-kb mNBC3 transcript only in skeletal muscle and heart. Burnham et al. (2000) stated that the NBC2 (Ishibashi et al., 1998) and mNBC3 (Pushkin et al., 1999) cDNAs share several kb of identical sequence. Although

the deduced protein sequences differ in their N and C termini and each protein contains an interior region not present in the other, the corresponding blocks share more than 99% identity. Thus, Burnham et al. (2000) suggested that NBC2 and mNBC3 are encoded by the same gene.

Burnham et al. (2000) isolated a human melanoma cell cDNA that encodes a protein containing elements previously thought to be characteristic of each of the variants NBC2 and mNBC3. Northern blot analysis of several human tissues using a probe specific to NBC2 detected expression mainly in lymph node and brain. Northern blot analysis using a probe specific to mNBC3 showed highest expression in skeletal muscle and heart and lower expression in lymph node, whole brain, adrenal gland, trachea, thyroid, stomach, pancreas, kidney, liver, lung, and placenta. Burnham et al. (2000) concluded that the melanoma cell, NBC2, and mNBC3 cDNAs represent 3 alternate transcripts of the SLC4A7 gene, which they called NBC2

[7885] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7886] Pushkin, A.; Abuladze, N.; Lee, I.; Newman, D.; Hwang, J.;

Kurtz, I. : Mapping of the human NBC3 (SLC4A7) gene to chromosome 3p22. Genomics 57: 321–322, 1999. Note: Correction: Genomics 58: 216 and 321–322, 1999. ; and

[7887] Soleimani, M.; Burnham, C. E. : Physiologic and molecular aspects of the Na(+):HCO(3-) cotransporter in health and disease processes. Kidney Int. 57: 371–384, 2000.

[7888] Further studies establishing the function and utilities of SLC4A7 are found in John Hopkins OMIM database record ID 603353, and in cited publications numbered 1083–108 and 7959 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Angiotensin Like 2 (AMOTL2, Accession NM_016201) is another VGAM66 host target gene. AMOTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL2 BINDING SITE, designated SEQ ID:18295, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7889] Another function of VGAM66 is therefore inhibition of Angiotensin Like 2 (AMOTL2, Accession NM_016201). Ac-

cordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL2. CG018 (Accession NM_052818) is another VGAM66 host target gene. CG018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CG018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CG018 BINDING SITE, designated SEQ ID:27406, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7890] Another function of VGAM66 is therefore inhibition of CG018 (Accession NM_052818). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CG018. KIAA0441 (Accession NM_014797) is another VGAM66 host target gene. KIAA0441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0441 BINDING SITE,

designated SEQ ID:16714, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7891] Another function of VGAM66 is therefore inhibition of KIAA0441 (Accession NM_014797). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0441. KIAA0470 (Accession NM_014812) is another VGAM66 host target gene. KIAA0470 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0470, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0470 BINDING SITE, designated SEQ ID:16778, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7892] Another function of VGAM66 is therefore inhibition of KIAA0470 (Accession NM_014812). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0470. KIAA1712 (Accession XM_041497) is another VGAM66 host target gene. KIAA1712 BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1712, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1712 BINDING SITE, designated SEQ ID:33541, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7893] Another function of VGAM66 is therefore inhibition of KIAA1712 (Accession XM_041497). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1712. NET-6 (Accession NM_014399) is another VGAM66 host target gene. NET-6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NET-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NET-6 BINDING SITE, designated SEQ ID:15742, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7894] Another function of VGAM66 is therefore inhibition of

NET-6 (Accession NM_014399). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NET-6. RCD-8 (Accession NM_014329) is another VGAM66 host target gene. RCD-8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RCD-8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RCD-8 BINDING SITE, designated SEQ ID:15639, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7895] Another function of VGAM66 is therefore inhibition of RCD-8 (Accession NM_014329). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RCD-8. LOC127281 (Accession XM_059128) is another VGAM66 host target gene. LOC127281 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC127281 BINDING SITE, designated SEQ ID:36891, to the nucleotide sequence of VGAM66 RNA, herein designated VGAM RNA, also designated SEQ ID:2777.

[7896] Another function of VGAM66 is therefore inhibition of LOC127281 (Accession XM_059128). Accordingly, utilities of VGAM66 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127281. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 67 (VGAM67) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7897] VGAM67 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM67 was detected is described hereinabove with reference to Figs. 1–8.

[7898] VGAM67 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[7899] VGAM67 gene encodes a VGAM67 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM67 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM67 precursor RNA is designated SEQ ID:53, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:53 is located at position 58356 relative to the genome of Invertebrate Iridescent Virus 6.

[7900] VGAM67 precursor RNA folds onto itself, forming VGAM67 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7901] An enzyme complex designated DICER COMPLEX, `dices` the VGAM67 folded precursor RNA into VGAM67 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM67 RNA is designated SEQ ID:2778, and is provided hereinbelow with reference to the sequence listing part.

[7902] VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM67 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7903] VGAM67 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM67 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of

each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM67 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7904] The complementary binding of VGAM67 RNA, herein designated VGAM RNA, to host target binding sites on VGAM67 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM67 host target RNA into VGAM67 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7905] It is appreciated that VGAM67 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM67 host target genes. The mRNA of each one of this plurality of VGAM67 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM67 RNA, herein designated VGAM RNA, and which when bound by VGAM67 RNA causes inhibition of translation of respective one or more VGAM67 host target proteins.

[7906] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM67 gene, herein designated VGAM GENE, on one or more VGAM67 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA

genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7907] It is yet further appreciated that a function of VGAM67 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM67 correlate with, and may be deduced from, the identity of the host target genes which VGAM67 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7908] Nucleotide sequences of the VGAM67 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM67 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM67 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM67 are further described hereinbelow with reference to Table 1.

[7909] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM67 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM67 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7910] As mentioned hereinabove with reference to Fig. 1, a function of VGAM67 gene, herein designated VGAM is inhibition of expression of VGAM67 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM67 correlate with, and may be deduced from, the identity of the target genes which VGAM67 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7911] Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529) is a VGAM67 host target gene. MLLT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT3 BINDING SITE, designated SEQ ID:10869, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7912] A function of VGAM67 is therefore inhibition of Myeloid/

lymphoid Or Mixed-lineage Leukemia (trithorax homolog, *Drosophila*); Translocated To, 3 (MLLT3, Accession NM_004529), a gene which is Serine and proline rich protein. Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT3. The function of MLLT3 has been established by previous studies. Nakamura et al. (1993) found that the AF4 gene on chromosome 4q21 (OMIM Ref. No. 159557) that is fused with the ALL1 gene (OMIM Ref. No. 159555) in patients with acute lymphoblastic leukemia and translocation t(4;11)(q21;q23) and the gene on chromosome 9 that is fused with the ALL1 gene on chromosome 11 in patients with leukemia and the t(9;11)(p22;q23) show high sequence homology with the ENL gene (OMIM Ref. No. 159556) on chromosome 19 which is fused to the ALL1 gene in patients with leukemia and the translocation t(11;19)(q23;p13). They found further that the protein products of the AF4, AF9, and ENL genes contained nuclear targeting sequences as well as serine-rich and proline-rich regions. Stretches abundant in basic amino acids were also present in the 3 proteins. These results indicated that the different proteins fused to ALL1 polypeptides in leukemia provide sim-

ilar functional domains. This gene is also symbolized MLLT3. The human AF9 gene is one of the most common fusion partner genes with the ALL1 gene at 11q23 (also called MLL), resulting in the t(9;11)(p22;q23). The AF9 gene is more than 100 kb, and 2 patient breakpoint cluster regions (BCRs) have been identified; BCR1 is within intron 4, previously called site A, whereas BCR2 or site B spans introns 7 and 8. Strissel et al. (2000) defined the exon–intron boundaries and identified several different structural elements in AF9, including a colocalizing in vivo DNA topo II cleavage site and an in vitro DNase I hypersensitive (DNase I HS) site in intron 7 in BCR2. Reversibility experiments demonstrated a religation of the topo II cleavage sites. In addition, 2 scaffold associated regions (SARs) are located centromeric to the topo II and DNase I HS cleavage sites and border breakpoint regions in 2 leukemic cell lines: SAR1 is located in intron 4, whereas SAR2 encompasses parts of exons 5–7. The authors thus demonstrated that the patient breakpoint regions of AF9 share the same structural elements as the MLL BCR, and they proposed a DNA breakage and repair model for non-homologous recombination between MLL and its partner genes, particularly AF9.

- [7913] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [7914] Nakamura, T.; Alder, H.; Gu, Y.; Prasad, R.; Canaani, O.; Kamada, N.; Gale, R. P.; Lange, B.; Crist, W. M.; Nowell, P. C.; Croce, C. M.; Canaani, E. : Genes on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia share sequence homology and/or common motifs. Proc. Nat. Acad. Sci. 90: 4631–4635, 1993. ; and
- [7915] Strissel, P. L.; Strick, R.; Tomek, R. J.; Roe, B. A.; Rowley, J. D.; Zeleznik–Le, N. J. : DNA structural properties of AF9 are similar to MLL and could act as recombination hot spots r.
- [7916] Further studies establishing the function and utilities of MLLT3 are found in John Hopkins OMIM database record ID 159558, and in cited publications numbered 3277 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430) is another VGAM67 host target gene. MN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MN1, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MN1 BINDING SITE, designated SEQ ID:8271, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7917] Another function of VGAM67 is therefore inhibition of Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MN1. A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274) is another VGAM67 host target gene. AKAP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP6 BINDING SITE, designated SEQ ID:10492, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7918] Another function of VGAM67 is therefore inhibition of A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274). Accordingly, utilities of VGAM67 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with AKAP6. DJ37E16.5 (Accession NM_020315) is another VGAM67 host target gene.

DJ37E16.5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DJ37E16.5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DJ37E16.5 BINDING SITE, designated SEQ ID:21579, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7919] Another function of VGAM67 is therefore inhibition of DJ37E16.5 (Accession NM_020315). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DJ37E16.5. FLJ20694 (Accession NM_017928) is another VGAM67 host target gene. FLJ20694 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20694 BINDING

SITE, designated SEQ ID:19603, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7920] Another function of VGAM67 is therefore inhibition of FLJ20694 (Accession NM_017928). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20694. KIAA0276 (Accession XM_048199) is another VGAM67 host target gene. KIAA0276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0276 BINDING SITE, designated SEQ ID:35138, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7921] Another function of VGAM67 is therefore inhibition of KIAA0276 (Accession XM_048199). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0276. KIAA0993 (Accession XM_034413) is another VGAM67 host target gene. KIAA0993 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0993, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0993 BINDING SITE, designated SEQ ID:32082, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7922] Another function of VGAM67 is therefore inhibition of KIAA0993 (Accession XM_034413). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0993. KIAA1056 (Accession NM_014894) is another VGAM67 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17045, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7923] Another function of VGAM67 is therefore inhibition of

KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. LOC257354 (Accession XM_170810) is another VGAM67 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45573, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7924] Another function of VGAM67 is therefore inhibition of LOC257354 (Accession XM_170810). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. LOC90198 (Accession XM_029882) is another VGAM67 host target gene. LOC90198 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC90198 BINDING SITE, designated SEQ ID:30957, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7925] Another function of VGAM67 is therefore inhibition of LOC90198 (Accession XM_029882). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90198. LOC91380 (Accession XM_038134) is another VGAM67 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32761, to the nucleotide sequence of VGAM67 RNA, herein designated VGAM RNA, also designated SEQ ID:2778.

[7926] Another function of VGAM67 is therefore inhibition of LOC91380 (Accession XM_038134). Accordingly, utilities of VGAM67 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91380. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 68 (VGAM68) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7927] VGAM68 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM68 was detected is described hereinabove with reference to Figs. 1–8.

[7928] VGAM68 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7929] VGAM68 gene encodes a VGAM68 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM68 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM68 precursor RNA is designated SEQ ID:54, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:54 is

located at position 27881 relative to the genome of Invertebrate Iridescent Virus 6.

[7930] VGAM68 precursor RNA folds onto itself, forming VGAM68 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7931] An enzyme complex designated DICER COMPLEX, `dices` the VGAM68 folded precursor RNA into VGAM68 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM68 RNA is designated SEQ ID:2779, and is provided hereinbelow with reference to the sequence listing part.

[7932] VGAM68 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM68 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7933] VGAM68 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM68 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM68 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM68 host target RNA, herein designated VGAM

HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7934] The complementary binding of VGAM68 RNA, herein designated VGAM RNA, to host target binding sites on VGAM68 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM68 host target RNA into VGAM68 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7935] It is appreciated that VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM68 host target genes. The mRNA of each one of this plurality of VGAM68 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM68 RNA, herein designated VGAM RNA, and which when bound by VGAM68 RNA causes inhibition of translation of respective one or more VGAM68 host target proteins.

[7936] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM68 gene, herein designated VGAM GENE, on one or more VGAM68 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7937] It is yet further appreciated that a function of VGAM68 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM68 correlate with, and may be deduced from, the identity of

the host target genes which VGAM68 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7938] Nucleotide sequences of the VGAM68 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM68 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM68 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM68 are further described hereinbelow with reference to Table 1.

[7939] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM68 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM68 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7940] As mentioned hereinabove with reference to Fig. 1, a function of VGAM68 gene, herein designated VGAM is inhibition of expression of VGAM68 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM68 correlate with, and may be deduced from, the identity of the target genes which VGAM68 binds and in-

hibits, and the function of these target genes, as elaborated hereinbelow.

[7941] Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM_001609) is a VGAM68 host target gene. ACADSB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACADSB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACADSB BINDING SITE, designated SEQ ID:7314, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7942] A function of VGAM68 is therefore inhibition of Acyl-Coenzyme A Dehydrogenase, Short/branched Chain (ACADSB, Accession NM_001609). Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACADSB. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529) is another VGAM68 host target gene. MLLT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT3 BINDING SITE, designated SEQ ID:10870, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7943] Another function of VGAM68 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529), a gene which is Serine and proline rich protein. Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT3. The function of MLLT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM67. Methylthioadenosine Phosphorylase (MTAP, Accession NM_002451) is another VGAM68 host target gene. MTAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of MTAP BINDING SITE, designated SEQ ID:8287, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7944] Another function of VGAM68 is therefore inhibition of Methylthioadenosine Phosphorylase (MTAP, Accession NM_002451), a gene which plays a major role in polyamine metabolism. Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTAP. The function of MTAP has been established by previous studies. Methylthioadenosine phosphorylase (EC 24.2.28) plays a major role in polyamine metabolism and is important for the salvage of both adenine and methionine. For example, as much as 97% of the endogenous adenine produced by human lymphoblasts in culture is formed by catabolism of methylthioadenosine (OMIM Ref. No. MeSAdo) by the phosphorylase. MeSAdo, a by-product of the synthesis of the polyamines spermidine and spermine, potently inhibits polyamine aminopropyltransferase reactions if not removed by the above phosphorylase reaction. MeSAdo phosphorylase is abundant in normal cells and tissues but lacking from many human and murine malignant cell lines

and from some human leukemias in vivo. Carrera et al. (1984) studied hybrids between MeSAdo phosphorylase-deficient mouse L cells and human fibroblasts to show that the structural gene (symbolized MSAP or MTAP) is located in the 9pter-q12 segment. This enzyme is missing in malignant cells in cases of lymphomatous acute lymphoblastic leukemia (OMIM Ref. No. 247640); many of these cases have abnormality of 9p22-p21 (Chilcote et al., 1985). As indicated by the findings of Olopade et al. (1992), the MTAP locus is centromeric to the cluster of interferon genes (e.g., 147640). Thus, the likely location of MTAP is 9p21. Nobori et al. (1996) cloned the MTAP gene and constructed a topologic map of the 9p21 region using YAC clones, pulsed-field gel electrophoresis, and sequence tagged-site PCR. The MTAP gene consists of 8 exons and 7 introns. Of 23 malignant cell lines deficient in MTAP protein, all but 1 had complete or partial deletions. Partial or total deletions of the MTAP gene were found in primary T-cell acute lymphoblastic leukemias. Within intron 4 they found a deletion breakpoint of partial deletions present in malignant cell lines and primary T-cell acute lymphoblastic leukemias. Starting from the centromeric end, the gene order on chromosome 9p21 was

found to be p15 (OMIM Ref. No. 600431)--p16--MTAP--IFNA (OMIM Ref. No. 147660)--IFNB. These results indicated to Nobori et al. (1996) that MTAP deficiency in cancer is primarily due to codeletion of the MTAP and p16 genes.

- [7945] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [7946] Carrera, C. J.; Eddy, R. L.; Shows, T. B.; Carson, D. A. : Assignment of the gene for methylthioadenosine phosphorylase to human chromosome 9 by mouse-human somatic cell hybridization. Proc. Nat. Acad. Sci. 81: 2665-2668, 1984. ; and
- [7947] Nobori, T.; Takabayashi, K.; Tran, P.; Orvis, L.; Batova, A.; Yu, A. L.; Carson, D. A. : Genomic cloning of methylthioadenosine phosphorylase: a purine metabolic enzyme deficient in mult.
- [7948] Further studies establishing the function and utilities of MTAP are found in John Hopkins OMIM database record ID 156540, and in cited publications numbered 12712-12718 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tryptophanyl-tRNA Synthetase (WARS, Accession

XM_041014) is another VGAM68 host target gene. WARS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WARS BINDING SITE, designated SEQ ID:33413, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7949] Another function of VGAM68 is therefore inhibition of Tryptophanyl-tRNA Synthetase (WARS, Accession XM_041014), a gene which is a tryptophanyl-tRNA synthetase. Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WARS. The function of WARS has been established by previous studies. Otani et al. (2002) showed that a recombinant form of a COOH-terminal fragment of tryptophanyl-tRNA synthetase is a potent antagonist of vascular endothelial growth factor (VEGF; 192240)-induced angiogenesis in a mouse model and of naturally occurring retinal angiogenesis in the neonatal mouse. Angiostatic activity was dose-dependent in both systems. The full-length protein was inactive as an antag-

onist of angiogenesis. The results suggested that fragments of tryptophanyl-tRNA synthetase, as naturally occurring and potentially nonimmunogenic anti-angiogenics, can be used for the treatment of neovascular eye diseases. In normal cells, human tryptophanyl-tRNA synthetase exists in 2 forms. The major form is the full-length protein, and the other is a truncated form in which most of the extra-NH₂-terminal domain is deleted because of alternative splicing of the pre-mRNA (Tolstrup et al., 1995; Turpaev et al., 1996), with met48 being deduced as the NH₂-terminal residue of the truncated form. The expression of the short form of WARS is highly stimulated in human cells by the addition of interferon-gamma (IFNG; 147570).

[7950] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7951] Otani, A.; Slike, B. M.; Dorrell, M. I.; Hood, J.; Kinder, K.; Ewalt, K. L.; Cheres, D.; Schimmel, P.; Friedlander, M. : A fragment of human TrpRS as a potent antagonist of ocular angiogenesis. Proc. Nat. Acad. Sci. 99: 178-183, 2002. ; and

[7952] Turpaev, K. T.; Zakhariev, V. M.; Sokolova, I. V.;

Narovlyansky, A. N.; Amchenkova, A. M.; Justesen, J.; Frolova, L. Y. : Alternative processing of the tryptophanyl-tRNA synthetase mRNA f.

[7953] Further studies establishing the function and utilities of WARS are found in John Hopkins OMIM database record ID 191050, and in cited publications numbered 10493-10495, 974 and 9765-9771 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Di-Ras2 (Accession NM_017594) is another VGAM68 host target gene. Di-Ras2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Di-Ras2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Di-Ras2 BINDING SITE, designated SEQ ID:19046, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7954] Another function of VGAM68 is therefore inhibition of Di-Ras2 (Accession NM_017594). Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Di-Ras2. RAB39, Member RAS Oncogene Family (RAB39, Accession

XM_084662) is another VGAM68 host target gene. RAB39 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB39 BINDING SITE, designated SEQ ID:37646, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7955] Another function of VGAM68 is therefore inhibition of RAB39, Member RAS Oncogene Family (RAB39, Accession XM_084662). Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB39. LOC158292 (Accession XM_098914) is another VGAM68 host target gene. LOC158292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158292 BINDING SITE, designated SEQ ID:41931, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2779.

[7956] Another function of VGAM68 is therefore inhibition of LOC158292 (Accession XM_098914). Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158292. LOC93380 (Accession XM_051020) is another VGAM68 host target gene. LOC93380 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93380 BINDING SITE, designated SEQ ID:35727, to the nucleotide sequence of VGAM68 RNA, herein designated VGAM RNA, also designated SEQ ID:2779.

[7957] Another function of VGAM68 is therefore inhibition of LOC93380 (Accession XM_051020). Accordingly, utilities of VGAM68 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 69 (VGAM69) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7958] VGAM69 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM69 was detected is described hereinabove with reference to Figs. 1–8.

[7959] VGAM69 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7960] VGAM69 gene encodes a VGAM69 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM69 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM69 precursor RNA is designated SEQ ID:55, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:55 is located at position 108748 relative to the genome of Invertebrate Iridescent Virus 6.

[7961] VGAM69 precursor RNA folds onto itself, forming VGAM69

folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7962] An enzyme complex designated DICER COMPLEX, `dices` the VGAM69 folded precursor RNA into VGAM69 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM69 RNA is designated SEQ ID:2780, and is provided hereinbelow with reference to the sequence listing part.

[7963] VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM69 host target RNA comprises three

regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[7964] VGAM69 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM69 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM69 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target bind-

ing sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[7965] The complementary binding of VGAM69 RNA, herein designated VGAM RNA, to host target binding sites on VGAM69 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM69 host target RNA into VGAM69 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7966] It is appreciated that VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM69 host target genes. The mRNA of each one of this plurality of VGAM69 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM69 RNA, herein designated VGAM RNA, and which when bound by VGAM69 RNA causes inhibition of translation of respective one or more VGAM69 host target proteins.

[7967] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM69 gene, herein designated VGAM GENE, on one or more VGAM69 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7968] It is yet further appreciated that a function of VGAM69 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM69 correlate with, and may be deduced from, the identity of the host target genes which VGAM69 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7969] Nucleotide sequences of the VGAM69 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM69 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM69 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM69 are further described hereinbelow with reference to Table 1.

[7970] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM69 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM69 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7971] As mentioned hereinabove with reference to Fig. 1, a function of VGAM69 gene, herein designated VGAM is inhibition of expression of VGAM69 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM69 correlate with, and may be deduced from, the identity of the target genes which VGAM69 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7972] DNA Cross-link Repair 1A (PSO2 homolog, *S. cerevisiae*)

(DCLRE1A, Accession XM_044815) is a VGAM69 host target gene. DCLRE1A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DCLRE1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCLRE1A BINDING SITE, designated SEQ ID:34280, to the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, also designated SEQ ID:2780.

[7973] A function of VGAM69 is therefore inhibition of DNA Cross-link Repair 1A (PSO2 homolog, *S. cerevisiae*) (DCLRE1A, Accession XM_044815). Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCLRE1A. Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM_045261) is another VGAM69 host target gene. LRRN3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LRRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRRN3 BINDING SITE, designated SEQ

ID:34398, to the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, also designated SEQ ID:2780.

[7974] Another function of VGAM69 is therefore inhibition of Leucine-rich Repeat Protein, Neuronal 3 (LRRN3, Accession XM_045261). Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRRN3. Phosphatidylserine Decarboxylase (PISD, Accession NM_014338) is another VGAM69 host target gene. PISD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PISD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PISD BINDING SITE, designated SEQ ID:15652, to the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, also designated SEQ ID:2780.

[7975] Another function of VGAM69 is therefore inhibition of Phosphatidylserine Decarboxylase (PISD, Accession NM_014338). Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PISD. RGPR (Accession

NM_033127) is another VGAM69 host target gene. RGPR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGPR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGPR BINDING SITE, designated SEQ ID:26970, to the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, also designated SEQ ID:2780.

[7976] Another function of VGAM69 is therefore inhibition of RGPR (Accession NM_033127). Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGPR. Solute Carrier Family 38, Member 1 (SLC38A1, Accession NM_030674) is another VGAM69 host target gene. SLC38A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC38A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC38A1 BINDING SITE, designated SEQ ID:25036, to the nucleotide sequence of VGAM69 RNA, herein designated VGAM RNA, also designated SEQ

ID:2780.

[7977] Another function of VGAM69 is therefore inhibition of Solute Carrier Family 38, Member 1 (SLC38A1, Accession NM_030674). Accordingly, utilities of VGAM69 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC38A1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 70 (VGAM70) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[7978] VGAM70 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM70 was detected is described hereinabove with reference to Figs. 1–8.

[7979] VGAM70 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[7980] VGAM70 gene encodes a VGAM70 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM70 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM70 precursor RNA is designated SEQ ID:56, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:56 is located at position 20882 relative to the genome of Invertebrate Iridescent Virus 6.

[7981] VGAM70 precursor RNA folds onto itself, forming VGAM70 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[7982] An enzyme complex designated DICER COMPLEX, `dices` the VGAM70 folded precursor RNA into VGAM70 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM70 RNA is designated SEQ ID:2781, and is provided hereinbelow with reference to the sequence listing part.

[7983] VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM70 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[7984] VGAM70 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM70 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM70 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[7985] The complementary binding of VGAM70 RNA, herein designated VGAM RNA, to host target binding sites on VGAM70 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM70 host target RNA into VGAM70 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[7986] It is appreciated that VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM70 host target genes. The mRNA of each one of this plurality of VGAM70 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM70 RNA, herein designated VGAM RNA, and which when bound by VGAM70 RNA causes inhibition of translation of respective one or more VGAM70 host target proteins.

[7987] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM70 gene, herein designated VGAM GENE, on one or more VGAM70 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[7988] It is yet further appreciated that a function of VGAM70 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM70 correlate with, and may be deduced from, the identity of the host target genes which VGAM70 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[7989] Nucleotide sequences of the VGAM70 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM70 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM70 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM70 are further described hereinbelow with reference to Table 1.

[7990] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM70 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM70 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[7991] As mentioned hereinabove with reference to Fig. 1, a function of VGAM70 gene, herein designated VGAM is inhibition of expression of VGAM70 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM70 correlate with, and may be deduced from, the identity of the target genes which VGAM70 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[7992] Chromosome 8 Open Reading Frame 1 (C8orf1, Accession NM_004337) is a VGAM70 host target gene. C8orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf1 BINDING SITE, designated SEQ ID:10532, to the nucleotide sequence of VGAM70 RNA, herein designated VGAM RNA, also designated SEQ ID:2781.

[7993] A function of VGAM70 is therefore inhibition of Chromosome 8 Open Reading Frame 1 (C8orf1, Accession NM_004337). Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf1. Carnitine O-

octanoyltransferase (CROT, Accession NM_021151) is another VGAM70 host target gene. CROT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CROT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CROT BINDING SITE, designated SEQ ID:22126, to the nucleotide sequence of VGAM70 RNA, herein designated VGAM RNA, also designated SEQ ID:2781.

[7994] Another function of VGAM70 is therefore inhibition of Carnitine O-octanoyltransferase (CROT, Accession NM_021151), a gene which CROT plays a crucial role in the beta-oxidation of branched-chain fatty acids including pristanic acid. Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CROT. The function of CROT has been established by previous studies. Carnitine octanoyltransferase (EC 2.3.1.137) is a carnitine acyltransferase that catalyzes the reversible transfer of fatty acyl groups between CoA and carnitine. This provides a crucial step in the transport of medium- and long-chain acyl-CoA out of the mammalian peroxisome to the cytosol and

mitochondria. See also CRAT (OMIM Ref. No. 600184). Van der Leij et al. (2000) reviewed the function, structural features, and phylogenetics of human carnitine acyltransferase genes, including CROT Using enzyme activity measurements of CROT expressed in a carnitine acetyltransferase-deficient yeast strain, Ferdinandusse et al. (1999) demonstrated that CROT efficiently converts a branched-chain fatty acyl-CoA (4,8-dimethylnonanoyl-CoA) to its corresponding carnitine ester. They hypothesized that CROT plays a crucial role in the beta-oxidation of branched-chain fatty acids including pristanic acid

[7995] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[7996] Ferdinandusse, S.; Mulders, J.; IJlst, L.; Denis, S.; Dacremont, G.; Waterham, H. R.; Wanders, R. J. A. : Molecular cloning and expression of human carnitine octanoyltransferase: evidence for its role in the peroxisomal beta-oxidation of branched-chain fatty acids. *Biochem. Biophys. Res. Commun.* 263: 213-218, 1999. ; and

[7997] van der Leij, F. R.; Huijkman, N. C. A.; Boomsma, C.; Kuipers, J. R. G.; Bartelds, B. : Genomics of the human carnitine acyltransferase genes. *Molec. Genet. Metab.* 71:

139–153, 2000.

[7998] Further studies establishing the function and utilities of CROT are found in John Hopkins OMIM database record ID 606090, and in cited publications numbered 612 and 7746 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PB1 (Accession NM_018165) is another VGAM70 host target gene. PB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PB1 BINDING SITE, designated SEQ ID:19984, to the nucleotide sequence of VGAM70 RNA, herein designated VGAM RNA, also designated SEQ ID:2781.

[7999] Another function of VGAM70 is therefore inhibition of PB1 (Accession NM_018165). Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PB1. Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007) is another VGAM70 host target gene. PLAGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL2 BINDING SITE, designated SEQ ID:34882, to the nucleotide sequence of VGAM70 RNA, herein designated VGAM RNA, also designated SEQ ID:2781.

[8000] Another function of VGAM70 is therefore inhibition of Pleiomorphic Adenoma Gene-like 2 (PLAGL2, Accession XM_047007). Accordingly, utilities of VGAM70 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 71 (VGAM71) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8001] VGAM71 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM71 was detected is described hereinabove with reference to Figs. 1-8.

[8002] VGAM71 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent

Virus 6. VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8003] VGAM71 gene encodes a VGAM71 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM71 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM71 precursor RNA is designated SEQ ID:57, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:57 is located at position 34908 relative to the genome of Invertebrate Iridescent Virus 6.

[8004] VGAM71 precursor RNA folds onto itself, forming VGAM71 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8005] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM71 folded precursor RNA into VGAM71 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM71 RNA is designated SEQ ID:2782, and is provided hereinbelow with reference to the sequence listing part.

[8006] VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM71 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8007] VGAM71 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide

sequence of VGAM71 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM71 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8008] The complementary binding of VGAM71 RNA, herein designated VGAM RNA, to host target binding sites on VGAM71 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM71 host target RNA into VGAM71 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[8009] It is appreciated that VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM71 host target genes. The mRNA of each one of this plurality of VGAM71 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM71 RNA, herein designated VGAM RNA, and which when bound by VGAM71 RNA causes inhibition of translation of respective one or more VGAM71 host target proteins.

[8010] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM71 gene, herein designated VGAM GENE, on one or more VGAM71 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression

of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8011] It is yet further appreciated that a function of VGAM71 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM71 correlate with, and may be deduced from, the identity of the host target genes which VGAM71 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8012] Nucleotide sequences of the VGAM71 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM71 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM71 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM71 are further described hereinbelow with reference to Table 1.

[8013] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM71 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM71 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8014] As mentioned hereinabove with reference to Fig. 1, a function of VGAM71 gene, herein designated VGAM is inhibition of expression of VGAM71 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM71 correlate with, and may be deduced from, the identity of the target genes which VGAM71 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8015] Cardiotrophin 1 (CTF1, Accession NM_001330) is a VGAM71 host target gene. CTF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTF1 BINDING SITE, designated SEQ ID:7012, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8016] A function of VGAM71 is therefore inhibition of Cardiotrophin 1 (CTF1, Accession NM_001330), a gene which may play a role in cardiac hypertrophy. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTF1. The function of CTF1 has been established by previous studies. Heart failure is a leading cause of mortality worldwide. A hallmark of the disease is dilated cardiac hypertrophy, which is accompanied by a reactivation of genes expressed in fetal heart development. Reasoning that fetal or embryonic growth factors may mediate the onset of cardiac hypertrophy, Pennica et al. (1995) coupled expression cloning with an embryonic stem cell-based model of cardiogenesis to isolate a 21.5-kD protein, cardiotrophin 1, that potently induces cardiac myocyte hypertrophy in vitro. Amino acid similarity data indicated that CT1 is a member of the family of cytokines that includes leukemia inhibitory factor (LIF; 159540), ciliary neurotrophic factor (CNTF; 118945), oncostatin M (OSM; 165095), interleukin 6 (IL6; 147620), and interleukin 11 (IL11; 147681). Several members of this family that are known to signal through the transmembrane protein gp130 (OMIM Ref. No. 162820) stimulate cardiac my-

ocyte hypertrophy, like cardiotrophin 1, suggesting that the gp130 signaling pathway may play a role in cardiac hypertrophy. The 1.4-kb CT1 mRNA is present in the heart and several other mouse tissues. Amyotrophic lateral sclerosis (ALS; 105400) is mainly a sporadic neurodegenerative disorder characterized by loss of cortical and spinal motoneurons. Some familial ALS (FALS) cases have been linked to dominant mutations in the gene encoding Cu/Zn superoxide dismutase (SOD1; 147450). Transgenic mice overexpressing a mutated form of human SOD1 with a gly93-to-ala substitution (147450.0008) develop progressive muscle wasting and paralysis as a result of spinal motoneuron loss and die at 5 to 6 months. Bordet et al. (2001) investigated the effects of neurotrophic factor gene delivery in this FALS model. Intramuscular injection of an adenoviral vector encoding CTF1 in SOD1(G93A) newborn mice delayed the onset of motor impairment as assessed in the rotarod test. By CTF1 treatment, axonal degeneration was slowed, skeletal muscle atrophy was largely reduced, and the time-course of motor impairment was significantly decreased.

[8017] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [8018] Pennica, D.; King, K. L.; Shaw, K. J.; Luis, E.; Rullamas, J.; Luoh, S.-M.; Darbonne, W. C.; Knutzon, D. S.; Yen, R.; Chien, K. R.; Baker, J. B.; Wood, W. I. : Expression cloning of cardiotrophin 1, a cytokine that induces cardiac myocyte hypertrophy. *Proc. Nat. Acad. Sci.* 92: 1142–1146, 1995. ; and
- [8019] Bordet, T.; Lesbordes, J.-C.; Rouhani, S.; Castelnau-Ptakhine, L.; Schmalbruch, H.; Haase, G.; Kahn, A. : Protective effects of cardiotrophin-1 adenoviral gene transfer on neuromuscular.
- [8020] Further studies establishing the function and utilities of CTF1 are found in John Hopkins OMIM database record ID 600435, and in cited publications numbered 12309–776 and 7677 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. NEBL (Accession NM_006393) is another VGAM71 host target gene. NEBL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NEBL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEBL BINDING SITE, designated SEQ ID:13102,

to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8021] Another function of VGAM71 is therefore inhibition of NEBL (Accession NM_006393). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEBL. Opioid Binding Protein/cell Adhesion Molecule-like (OPCML, Accession NM_002545) is another VGAM71 host target gene. OPCML BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPCML, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPCML BINDING SITE, designated SEQ ID:8397, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8022] Another function of VGAM71 is therefore inhibition of Opioid Binding Protein/cell Adhesion Molecule-like (OPCML, Accession NM_002545), a gene which may function as a GPI-anchored neural cell adhesion molecule. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with OPCML. The function of OPCML has been established by previous studies. OBCAM, also designated OPCML, is a protein that binds opioid alkaloids in the presence of acidic lipids, exhibiting selectivity for mu ligands. It shares structural homology with members of the immunoglobulin protein superfamily, most notably with cell-adhesion molecules. Analysis of the amino acid sequence indicates that it is an extracellularly located molecule, and the presence of a hydrophobic C terminus suggests that it may be inserted into the cell membrane through phosphatidylinositol linkage. Shark and Lee (1995) stated that, due to the lack of transmembrane domains necessary for signal transduction, it is improbable that OBCAM acts independently as an opioid receptor; more likely, it plays an important accessory role in opioid receptor function. OBCAM was first purified from bovine brain by Cho et al. (1986). The gene was mapped to mouse chromosome 9, and from linkage homology data it was predicted that its human counterpart would lie on either 19p or 11q22-qter (Chakraborti et al., 1993). Shark and Lee (1995) used DNA primers derived from rat OBCAM cDNA to PCR-amplify a 403-bp fragment from a human brain cDNA library. The fragment was cloned, se-

quenced, and used as a hybridization probe to screen the library to obtain a cDNA fragment, including a complete open reading frame of 1,038 bp. Sequence analysis of the ORF revealed 93% identity to the rat OBCAM cDNA at the nucleotide level and 98% identity at the deduced amino acid sequence level. By hybridization to a somatic cell hybrid panel, they mapped the gene to chromosome 11. They noted that the gene for neural cell adhesion molecule (NCAM; 116930) and other proteins of similar structure that are expressed in the nervous system also map to 11q22–q23.

[8023] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8024] Chakraborti, A.; Lippman, D. L.; Loh, H. H.; Kozak, C. A.; Lee, N. M. : Genetic mapping of opioid binding protein gene(s) to mouse chromosome 9. *Mammalian Genome* 4: 179–182, 1993. ; and

[8025] Shark, K. B.; Lee, N. M. : Cloning, sequencing and localization to chromosome 11 of a cDNA encoding a human opioid-binding cell adhesion molecule (OBCAM). *Gene* 155: 213–217, 1995.

[8026] Further studies establishing the function and utilities of

OPCML are found in John Hopkins OMIM database record ID 600632, and in cited publications numbered 6836–6838 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Alpha 9 (PCDHA9, Accession NM_014005) is another VGAM71 host target gene. PCDHA9 BINDING SITE1 and PCDHA9 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHA9, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE1 and PCDHA9 BINDING SITE2, designated SEQ ID:15215 and SEQ ID:25607 respectively, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8027] Another function of VGAM71 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_014005), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 has been established by previous studies. Cadherins are

calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHA9 is a member of the alpha cluster of protocadherin genes on 5q31. By screening a brain cDNA library for sequences with the potential to encode large proteins, Nagase et al. (1997) identified a cDNA encoding PCDHA9, which they termed KIAA0345. The deduced protein has 842 amino acids. RT-PCR analysis detected strongest expression of KIAA0345 in kidney and testis, followed by brain, lung, pancreas, and ovary.

[8028] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8029] Nagase, T.; Ishikawa, I.; Nakajima, D.; Ohira, M.; Seki, N.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; O'Hara, O. : Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 4: 141-150, 1997. ; and

[8030] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; Myers, R. M.; Maniatis, T. : Comparative DNA sequence anal-

ysis of mouse and.

[8031] Further studies establishing the function and utilities of PCDHA9 are found in John Hopkins OMIM database record ID 606315, and in cited publications numbered 730 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB4A, Member RAS Oncogene Family (RAB4A, Accession NM_004578) is another VGAM71 host target gene. RAB4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB4A BINDING SITE, designated SEQ ID:10926, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8032] Another function of VGAM71 is therefore inhibition of RAB4A, Member RAS Oncogene Family (RAB4A, Accession NM_004578), a gene which is involved in protein transport. Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB4A. The function of RAB4A has been established by previous studies. The mammalian

RAB proteins show striking similarities to the *S. cerevisiae* YPT1 and SEC4 proteins, Ras-related GTP-binding proteins involved in the regulation of secretion. Zahraoui et al. (1989) isolated cDNAs encoding RAB4 and several other human RAB proteins. See RAB5A (OMIM Ref. No. 179512). The predicted 213-amino acid human RAB4 protein shares 98% and 50% identity with rat Rab4 and human RAB2, respectively. Northern blot analysis revealed that the RAB4 gene was expressed weakly as 1.8-, 3.1-, and 3.6-kb mRNAs in a human fibroblast cell line. By in situ hybridization, Rousseau-Merck et al. (1991) assigned the RAB4 gene to 1q42-q43. Barbosa et al. (1995) referred to this locus as RAV4A and mapped the mouse homolog by interspecific backcross analysis to the distal end of mouse chromosome 8. The authors mapped Rab4b to proximal mouse chromosome 7. They also reported that 4 additional members of the mouse Rab gene family exist on mouse chromosomes 2, 9, 12, and 13.

[8033] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8034] Barbosa, M. D. F. S.; Johnson, S. A.; Achey, K.; Gutierrez, M.; Wakeland, E. K.; Zerial, M.; Kingsmore, S. F. : The Rab

protein family: genetic mapping of six Rab genes in the mouse. Genomics 30: 439–444, 1995. ; and

[8035] Zahraoui, A.; Touchot, N.; Chardin, P.; Tavitian, A. : The human rab genes encode a family of GTP-binding proteins related to yeast YPT1 and SEC4 products involved in secretion. J. Biol.

[8036] Further studies establishing the function and utilities of RAB4A are found in John Hopkins OMIM database record ID 179511, and in cited publications numbered 2540–254 and 2722 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ADP-ribosylation Factor GTPase Activating Protein 3 (ARFGAP3, Accession NM_014570) is another VGAM71 host target gene. ARFGAP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARFGAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARFGAP3 BINDING SITE, designated SEQ ID:15926, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8037] Another function of VGAM71 is therefore inhibition of

ADP-ribosylation Factor GTPase Activating Protein 3 (ARFGAP3, Accession NM_014570). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF-GAP3. BOP (Accession XM_097915) is another VGAM71 host target gene. BOP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BOP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BOP BINDING SITE, designated SEQ ID:41211, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8038] Another function of VGAM71 is therefore inhibition of BOP (Accession XM_097915). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BOP. Chemokine (C-C motif) Receptor 1 (CCR1, Accession NM_001295) is another VGAM71 host target gene. CCR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CCR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR1 BINDING SITE, designated SEQ ID:6976, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8039] Another function of VGAM71 is therefore inhibition of Chemokine (C-C motif) Receptor 1 (CCR1, Accession NM_001295). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR1. DKFZP434F1735 (Accession NM_015590) is another VGAM71 host target gene. DKFZP434F1735 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434F1735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F1735 BINDING SITE, designated SEQ ID:17856, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8040] Another function of VGAM71 is therefore inhibition of DKFZP434F1735 (Accession NM_015590). Accordingly, utilities of VGAM71 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with DKFZP434F1735. DKFZP434P211 (Accession NM_014549) is another VGAM71 host target gene. DKFZP434P211 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434P211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P211 BINDING SITE, designated SEQ ID:15871, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8041] Another function of VGAM71 is therefore inhibition of DKFZP434P211 (Accession NM_014549). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P211. EKI1 (Accession NM_018638) is another VGAM71 host target gene. EKI1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EKI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EKI1 BINDING SITE, desig-

nated SEQ ID:20709, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8042] Another function of VGAM71 is therefore inhibition of EKI1 (Accession NM_018638). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EKI1. Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962) is another VGAM71 host target gene. KCNT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNT1 BINDING SITE, designated SEQ ID:30979, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8043] Another function of VGAM71 is therefore inhibition of Potassium Channel, Subfamily T, Member 1 (KCNT1, Accession XM_029962). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNT1. KIAA1046

(Accession NM_014928) is another VGAM71 host target gene. KIAA1046 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1046 BINDING SITE, designated SEQ ID:17222, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8044] Another function of VGAM71 is therefore inhibition of KIAA1046 (Accession NM_014928). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1046. KIAA1719 (Accession XM_042936) is another VGAM71 host target gene. KIAA1719 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1719 BINDING SITE, designated SEQ ID:33826, to the nucleotide sequence of VGAM71 RNA, herein designated

VGAM RNA, also designated SEQ ID:2782.

[8045] Another function of VGAM71 is therefore inhibition of KIAA1719 (Accession XM_042936). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1719. MGC20253 (Accession NM_144583) is another VGAM71 host target gene. MGC20253 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20253, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20253 BINDING SITE, designated SEQ ID:29400, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8046] Another function of VGAM71 is therefore inhibition of MGC20253 (Accession NM_144583). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20253. MGC5566 (Accession NM_024049) is another VGAM71 host target gene. MGC5566 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5566, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5566 BINDING SITE, designated SEQ ID:23487, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8047] Another function of VGAM71 is therefore inhibition of MGC5566 (Accession NM_024049). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5566. SDF1 (Accession XM_165565) is another VGAM71 host target gene. SDF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDF1 BINDING SITE, designated SEQ ID:43692, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8048] Another function of VGAM71 is therefore inhibition of SDF1 (Accession XM_165565). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SDF1.

Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131) is another VGAM71 host target gene. SRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRF BINDING SITE, designated SEQ ID:9106, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8049] Another function of VGAM71 is therefore inhibition of Serum Response Factor (c-fos serum response element-binding transcription factor) (SRF, Accession NM_003131). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRF. Tripartite Motif-containing 26 (TRIM26, Accession NM_003449) is another VGAM71 host target gene. TRIM26 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND-

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM26 BINDING SITE, designated SEQ ID:9502, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8050] Another function of VGAM71 is therefore inhibition of Tripartite Motif-containing 26 (TRIM26, Accession NM_003449). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM26. LOC114971 (Accession XM_054936) is another VGAM71 host target gene. LOC114971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114971 BINDING SITE, designated SEQ ID:36211, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8051] Another function of VGAM71 is therefore inhibition of LOC114971 (Accession XM_054936). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC114971. LOC148189 (Accession XM_086087) is another VGAM71 host target gene. LOC148189 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148189 BINDING SITE, designated SEQ ID:38488, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8052] Another function of VGAM71 is therefore inhibition of LOC148189 (Accession XM_086087). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148189. LOC151121 (Accession XM_087102) is another VGAM71 host target gene. LOC151121 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151121 BINDING SITE, designated SEQ ID:39054, to

the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8053] Another function of VGAM71 is therefore inhibition of LOC151121 (Accession XM_087102). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151121. LOC151473 (Accession XM_087215) is another VGAM71 host target gene. LOC151473 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151473, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151473 BINDING SITE, designated SEQ ID:39124, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8054] Another function of VGAM71 is therefore inhibition of LOC151473 (Accession XM_087215). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151473. LOC200734 (Accession XM_114286) is another VGAM71 host target gene. LOC200734 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC200734, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200734 BINDING SITE, designated SEQ ID:42845, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8055] Another function of VGAM71 is therefore inhibition of LOC200734 (Accession XM_114286). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200734. LOC221943 (Accession XM_168343) is another VGAM71 host target gene. LOC221943 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221943, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221943 BINDING SITE, designated SEQ ID:45117, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8056] Another function of VGAM71 is therefore inhibition of LOC221943 (Accession XM_168343). Accordingly, utilities

of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221943. LOC257494 (Accession XM_175212) is another VGAM71 host target gene. LOC257494 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257494 BINDING SITE, designated SEQ ID:46689, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8057] Another function of VGAM71 is therefore inhibition of LOC257494 (Accession XM_175212). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257494. LOC91522 (Accession XM_038953) is another VGAM71 host target gene. LOC91522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC91522 BINDING SITE, designated SEQ ID:32963, to the nucleotide sequence of VGAM71 RNA, herein designated VGAM RNA, also designated SEQ ID:2782.

[8058] Another function of VGAM71 is therefore inhibition of LOC91522 (Accession XM_038953). Accordingly, utilities of VGAM71 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91522. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 72 (VGAM72) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8059] VGAM72 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM72 was detected is described hereinabove with reference to Figs. 1–8.

[8060] VGAM72 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8061] VGAM72 gene encodes a VGAM72 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM72 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM72 precursor RNA is designated SEQ ID:58, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:58 is located at position 19212 relative to the genome of Invertebrate Iridescent Virus 6.

[8062] VGAM72 precursor RNA folds onto itself, forming VGAM72 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8063] An enzyme complex designated DICER COMPLEX, `dices` the VGAM72 folded precursor RNA into VGAM72 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM72 RNA is designated SEQ ID:2783, and is provided hereinbelow with reference to the sequence listing part.

[8064] VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM72 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8065] VGAM72 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM72 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration,

Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM72 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8066] The complementary binding of VGAM72 RNA, herein designated VGAM RNA, to host target binding sites on VGAM72 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM72 host target RNA into VGAM72 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8067] It is appreciated that VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM72 host target genes. The mRNA of each one of this plurality of VGAM72 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM72 RNA, herein designated VGAM RNA, and which when bound by VGAM72 RNA causes inhibition of translation of respective one or more VGAM72 host target proteins.

[8068] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM72 gene, herein designated VGAM GENE, on one or more VGAM72 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective:

Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8069] It is yet further appreciated that a function of VGAM72 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM72 correlate with, and may be deduced from, the identity of the host target genes which VGAM72 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8070] Nucleotide sequences of the VGAM72 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM72 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM72 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM72 are further described hereinbelow with reference to Table 1.

[8071] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM72 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM72 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[8072] As mentioned hereinabove with reference to Fig. 1, a function of VGAM72 gene, herein designated VGAM is inhibition of expression of VGAM72 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM72 correlate with, and may be deduced from, the identity of the target genes which VGAM72 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8073] SRY (sex determining region Y)-box 12 (SOX12, Accession NM_006943) is a VGAM72 host target gene. SOX12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOX12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOX12 BINDING SITE, designated SEQ ID:13832, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8074] A function of VGAM72 is therefore inhibition of SRY (sex determining region Y)-box 12 (SOX12, Accession NM_006943). Accordingly, utilities of VGAM72 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with SOX12. Chromosome 21 Open Reading Frame 55 (C21orf55, Accession NM_017833) is another VGAM72 host target gene. C21orf55 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C21orf55, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf55 BINDING SITE, designated SEQ ID:19499, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8075] Another function of VGAM72 is therefore inhibition of Chromosome 21 Open Reading Frame 55 (C21orf55, Accession NM_017833). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf55. MGC2452 (Accession NM_032644) is another VGAM72 host target gene. MGC2452 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of MGC2452 BINDING SITE, designated SEQ ID:26370, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8076] Another function of VGAM72 is therefore inhibition of MGC2452 (Accession NM_032644). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2452. Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM_005446) is another VGAM72 host target gene. P2RXL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P2RXL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RXL1 BINDING SITE, designated SEQ ID:11926, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8077] Another function of VGAM72 is therefore inhibition of Purinergic Receptor P2X-like 1, Orphan Receptor (P2RXL1, Accession NM_005446). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with P2RXL1. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM_028840) is another VGAM72 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30764, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8078] Another function of VGAM72 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM_028840). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R16B. LOC255328 (Accession XM_172920) is another VGAM72 host target gene. LOC255328 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC255328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC255328 BINDING SITE, designated SEQ ID:46178, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8079] Another function of VGAM72 is therefore inhibition of LOC255328 (Accession XM_172920). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255328. LOC90509 (Accession XM_032209) is another VGAM72 host target gene. LOC90509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90509 BINDING SITE, designated SEQ ID:31611, to the nucleotide sequence of VGAM72 RNA, herein designated VGAM RNA, also designated SEQ ID:2783.

[8080] Another function of VGAM72 is therefore inhibition of LOC90509 (Accession XM_032209). Accordingly, utilities of VGAM72 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90509. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 73 (VGAM73) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8081] VGAM73 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM73 was detected is described hereinabove with reference to Figs. 1–8.

[8082] VGAM73 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8083] VGAM73 gene encodes a VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM73 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM73 precursor RNA is designated SEQ ID:59, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:59 is

located at position 155229 relative to the genome of Invertebrate Iridescent Virus 6.

[8084] VGAM73 precursor RNA folds onto itself, forming VGAM73 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8085] An enzyme complex designated DICER COMPLEX, `dices` the VGAM73 folded precursor RNA into VGAM73 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM73 RNA is designated SEQ ID:2784, and is provided hereinbelow with reference to the sequence listing part.

[8086] VGAM73 host target gene, herein designated VGAM HOST

TARGET GENE, encodes a corresponding messenger RNA, VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM73 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8087] VGAM73 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM73 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM73 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM73 host target RNA, herein designated VGAM

HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8088] The complementary binding of VGAM73 RNA, herein designated VGAM RNA, to host target binding sites on VGAM73 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM73 host target RNA into VGAM73 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8089] It is appreciated that VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM73 host target genes. The mRNA of each one of this plurality of VGAM73 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM73 RNA, herein designated VGAM RNA, and which when bound by VGAM73 RNA causes inhibition of translation of respective one or more VGAM73 host target proteins.

[8090] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM73 gene, herein designated VGAM GENE, on one or more VGAM73 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8091] It is yet further appreciated that a function of VGAM73 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM73 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM73 correlate with, and may be deduced from, the identity of

the host target genes which VGAM73 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8092] Nucleotide sequences of the VGAM73 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM73 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM73 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM73 are further described hereinbelow with reference to Table 1.

[8093] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM73 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM73 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8094] As mentioned hereinabove with reference to Fig. 1, a function of VGAM73 gene, herein designated VGAM is inhibition of expression of VGAM73 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM73 correlate with, and may be deduced from, the identity of the target genes which VGAM73 binds and in-

hibits, and the function of these target genes, as elaborated hereinbelow.

[8095] Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858) is a VGAM73 host target gene. COL19A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL19A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL19A1 BINDING SITE, designated SEQ ID:7592, to the nucleotide sequence of VGAM73 RNA, herein designated VGAM RNA, also designated SEQ ID:2784.

[8096] A function of VGAM73 is therefore inhibition of Collagen, Type XIX, Alpha 1 (COL19A1, Accession NM_001858), a gene which may act as a cross-bridge between fibrils and other extracellular matrix molecules. Accordingly, utilities of VGAM73 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL19A1. The function of COL19A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM19. Dynein, Cytoplasmic, Interme-

diate Polypeptide 1 (DNCl1, Accession XM_165838) is another VGAM73 host target gene. DNCl1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNCl1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNCl1 BINDING SITE, designated SEQ ID:43776, to the nucleotide sequence of VGAM73 RNA, herein designated VGAM RNA, also designated SEQ ID:2784.

[8097] Another function of VGAM73 is therefore inhibition of Dynein, Cytoplasmic, Intermediate Polypeptide 1 (DNCl1, Accession XM_165838). Accordingly, utilities of VGAM73 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNCl1. HSPC031 (Accession NM_016101) is another VGAM73 host target gene. HSPC031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC031 BINDING SITE, designated SEQ ID:18185, to the nucleotide sequence of VGAM73 RNA,

herein designated VGAM RNA, also designated SEQ ID:2784.

[8098] Another function of VGAM73 is therefore inhibition of HSPC031 (Accession NM_016101). Accordingly, utilities of VGAM73 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC031. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 74 (VGAM74) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8099] VGAM74 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM74 was detected is described hereinabove with reference to Figs. 1–8.

[8100] VGAM74 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Invertebrate Iridescent Virus 6. VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8101] VGAM74 gene encodes a VGAM74 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM74 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM74 precursor RNA is designated SEQ ID:60, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:60 is located at position 202596 relative to the genome of Invertebrate Iridescent Virus 6.

[8102] VGAM74 precursor RNA folds onto itself, forming VGAM74 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8103] An enzyme complex designated DICER COMPLEX, `dices` the VGAM74 folded precursor RNA into VGAM74 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM74 RNA is designated SEQ ID:2785, and is provided hereinbelow with reference to the sequence listing part.

[8104] VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM74 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[8105] VGAM74 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM74 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM74 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8106] The complementary binding of VGAM74 RNA, herein designated VGAM RNA, to host target binding sites on VGAM74 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM74 host target RNA into VGAM74 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8107] It is appreciated that VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM74 host target genes. The mRNA of each one of this plurality of VGAM74 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM74 RNA, herein designated VGAM RNA, and which when bound by VGAM74 RNA causes inhibition of translation of respective one or more VGAM74 host target proteins.

[8108] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM74 gene, herein designated VGAM GENE, on one or more VGAM74 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8109] It is yet further appreciated that a function of VGAM74 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of viral infection by Invertebrate Iridescent Virus 6. Specific functions, and accordingly utilities, of VGAM74 correlate with, and may be deduced from, the identity of the host target genes which VGAM74 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8110] Nucleotide sequences of the VGAM74 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM74 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM74 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM74 are further described hereinbelow with reference to Table 1.

[8111] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM74 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM74 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8112] As mentioned hereinabove with reference to Fig. 1, a function of VGAM74 gene, herein designated VGAM is inhibition of expression of VGAM74 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM74 correlate with, and may be deduced from, the identity of the target genes which VGAM74 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8113] APPL (Accession NM_012096) is a VGAM74 host target gene. APPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APPL BINDING SITE, designated SEQ ID:14400, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8114] A function of VGAM74 is therefore inhibition of APPL (Accession NM_012096). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APPL. B-cell CLL/lymphoma 9 (BCL9, Accession NM_004326) is another VGAM74 host target gene. BCL9 BINDING SITE is HOST

TARGET binding site found in the 5' untranslated region of mRNA encoded by BCL9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL9 BINDING SITE, designated SEQ ID:10522, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8115] Another function of VGAM74 is therefore inhibition of B-cell CLL/lymphoma 9 (BCL9, Accession NM_004326), a gene which recruits of PYGO to the nuclear beta-catenin-TCF complex in Wnt/Wingless signaling. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL9. The function of BCL9 has been established by previous studies. WNT (see OMIM Ref. No. 602863) signaling controls many fundamental processes during animal development. WNT transduction is mediated by the association of beta-catenin (OMIM Ref. No. 116806) with nuclear TCF (e.g., LEF1; 153245) DNA-binding factors. Kramps et al. (2002) identified 2 segment polarity genes in *Drosophila*, legless (Lgs), and pygopus (Pygo), and showed that their products are required for

WNT signal transduction at the level of nuclear beta-catenin. Lgs encodes the homolog of human BCL9, and the authors provided genetic and molecular evidence that these proteins exert their function by physically linking Pygo to beta-catenin. Kramps et al. (2002) identified 2 human homologs of the Drosophila Pygo gene, PYGO1 (OMIM Ref. No. 606902) and PYGO2 (OMIM Ref. No. 606903), that possess a highly conserved PHD finger that interacts with homology domain-1 (HD1) of BCL9. The findings suggested that the recruitment of PYGO permits beta-catenin to transcriptionally activate WNT target genes and raised the possibility that a deregulation of these events may play a causal role in the development of B-cell malignancies. Studying a cell line (OMIM Ref. No. CEMO-1) from a patient with precursor-B-cell acute lymphoblastic leukemia with a t(1;14)(q21;q32), Willis et al. (1998) identified a fusion partner of the IGHJ gene (OMIM Ref. No. 147010) on 14q. One allele showed novel sequences upstream of JH5 with no homology to either IGH or any other sequence in databases. Using a single-copy restriction fragment immediately 5-prime of JH5, PAC clones were isolated and mapped to 1q21 on normal metaphases by fluorescence in situ hybridization, con-

firming that this allele represented the translocation breakpoint. Sequence analysis of the 1q21 restriction fragment showed identity with an expressed sequenced tag, and this probe was therefore used to probe Northern blots.

- [8116] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8117] Kramps, T.; Peter, O.; Brunner, E.; Nellen, D.; Froesch, B.; Chatterjee, S.; Murone, M.; Zullig, S.; Basler, K. : Wnt/Wingless signaling requires BCL9/legless-mediated recruitment of pygopus to the nuclear beta-catenin-TCF complex. Cell 109: 47–60, 2002. ; and
- [8118] Willis, T. G.; Zalcberg, I. R.; Coignet, L. J. A.; Wlodarska, M.; Stul, D. M.; Jadayel, D. M.; Bastard, C.; Treleaven, J. G.; Catovsky, D.; Silva, M. L. M.; Dyer, M. J. S. : Molecular c.
- [8119] Further studies establishing the function and utilities of BCL9 are found in John Hopkins OMIM database record ID 602597, and in cited publications numbered 8254–8255 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 2 (CYP1A2, Accession NM_000761) is another VGAM74 host

target gene. CYP1A2 BINDING SITE1 and CYP1A2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CYP1A2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A2 BINDING SITE1 and CYP1A2 BINDING SITE2, designated SEQ ID:6412 and SEQ ID:34256 respectively, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8120] Another function of VGAM74 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 2 (CYP1A2, Accession NM_000761), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A2. The function of CYP1A2 has been established by previous studies. P1-450 (CYP1A1; 108330) and P3-450 are 2 members of the dioxin-inducible P450 gene family. Jaiswal et al. (1987) determined the cDNA (3,064 bp) and protein (515 residues; M(r) = 58,294) sequences of P3-450. They showed by study of somatic cell hybrids that both the

P3-450 and the P1-450 loci reside on human chromosome 15. In the mouse and hamster, the 2 genes are located near the equivalent of the mannosephosphate isomerase (MPI) locus (OMIM Ref. No. 154550). The same may be true in man; MPI is located in the region 15q22-qter. The 2 CYP1 genes are within 25 kb of each other and probably are not separated by other genes (Nebert, 1988). The enzyme involved in O-deethylation of phenacetin is 1 of 9 forms of cytochrome P-450 that have been purified to electrophoretic homogeneity from human liver microsomes (Guengerich et al., 1986). Phenacetin O-deethylase differs from another cytochrome P-450 enzyme that shows genetic polymorphism, debrisoquine 4-hydroxylase (OMIM Ref. No. 124030), in molecular mass, amino acid composition, catalytic activity, and immunochemical properties. Butler et al. (1989) reviewed the evidence that phenacetin O-deethylase, otherwise known as P450(PA), is the product of the CYP1A2 gene. Devonshire et al. (1983) demonstrated a genetic polymorphism for phenacetin O-deethylation, with 5 to 10% of the population deficient in this activity. Cigarette smoking has been shown to increase microsomal phenacetin O-deethylase activity (Sesardic et al., 1988). Butler et al.

(1989) reported that human hepatic microsomal caffeine 3-demethylation, the initial major step in caffeine bio-transformation in humans, is selectively catalyzed by this cytochrome P-450. Estimation of caffeine 3-demethylation activity in humans may be useful in the characterization of arylamine N-oxidation phenotypes and in the assessment of whether or not the hepatic levels of this cytochrome, as affected by environmental or genetic factors, contribute to interindividual differences in susceptibility to arylamine-induced cancers. Smokers have been demonstrated to have increased rates of caffeine disposition, with plasma half lives one-half that of non-smokers. Furthermore, rates of caffeine metabolism vary between individuals, as caffeine half-life values ranging from 1.5 to 9.5 hours have been reported. Buters et al. (1996) showed that in mice the clearance of caffeine is determined primarily by CYP1A2.

[8121] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8122] Butler, M. A.; Iwasaki, M.; Guengerich, F. P.; Kadlubar, F. F. : Human cytochrome P-450(PA) (P-450IA2), the phenacetin O-deethylase, is primarily responsible for the

hepatic 3-demethylation of caffeine and N-oxidation of carcinogenic arylamines. Proc. Nat. Acad. Sci. 86: 7696-7700, 1989. ; and

[8123] Christiansen, L.; Bygum, A.; Jensen, A.; Thomsen, K.; Brandrup, F.; Horder, M.; Petersen, N. E. : Association between CYP1A2 polymorphism and susceptibility to porphyria cutanea tarda.

[8124] Further studies establishing the function and utilities of CYP1A2 are found in John Hopkins OMIM database record ID 124060, and in cited publications numbered 11772-11775, 3682, 11776-1177 and 12761-11782 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is another VGAM74 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20736, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8125] Another function of VGAM74 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 has been established by previous studies. Millar et al. (2000) isolated and sequenced the breakpoints on chromosomes 1 and 11 in the Scottish family carrying the translocation, and by sequence analysis concluded that no genes were within the region surrounding the chromosome 11 breakpoint. The authors found that, by contrast, the corresponding region on chromosome 1 was gene-dense and that not 1, but 2, novel genes were directly disrupted by the translocation. They named these genes 'disrupted in schizophrenia' 1 and 2 (DISC1 and DISC2, 606271). The major DISC1 transcript is approximately 7.5 kb, contains an open reading frame encoding 854 amino acids, and is ubiquitously expressed. The protein is predicted to consist of a globular N-terminal domain(s) and helical C-terminal domain that has the potential to form a coiled-coil by interaction with another protein(s). Similar structures are thought to be

present in a variety of unrelated proteins that are known to function in the nervous system. The putative structure of the protein encoded by DISC1 is therefore compatible with a role in the nervous system. DISC2 apparently specifies a single exon thought to be a noncoding RNA molecule that is antisense to DISC1, an arrangement that has been observed at other loci where the antisense RNA may regulate expression of the sense gene. The authors concluded that DISC1 and DISC2 should be considered formal candidate genes for susceptibility to psychiatric illness. The family studied by St. Clair et al. (1990) and Millar et al. (2000) was originally ascertained by Jacobs et al. (1970), who reported the translocation in the proband, who had adolescent conduct disorder, and in members of 4 generations of the extended family. Blackwood et al. (2001) provided a follow-up. Of the 87 members of the family who were karyotyped, 37 carried the translocation. A psychiatric diagnosis was reached in 29 carriers, 38 noncarriers, and the 2 founders (who were not karyotyped). The range of symptoms in this family crossed traditional diagnostic boundaries, and the locus identified by the breakpoint on 1q42 appeared to be implicated in either schizophrenia or bipolar disorder. Furthermore,

Blackwood (2000) reported abnormalities in the auditory P300 event-related potential, which showed prolonged latency and reduced amplitude in affected members of the family.

[8126] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8127] Blackwood, D. H. R.; Fordyce, A.; Walker, M. T.; St. Clair, D. M.; Porteous, D. J.; Muir, W. J. : Schizophrenia and affective disorders--cosegregation with a translocation at chromosome 1q42 that directly disrupts brain-expressed genes: clinical and P300 findings in a family. *Am. J. Hum. Genet.* 69: 428–433, 2001. ; and

[8128] Ekelund, J.; Hovatta, I.; Parker, A.; Paunio, T.; Varilo, T.; Martin, R.; Suhonen, J.; Ellonen, P.; Chan, G.; Sinsheimer, J. S.; Sobel, E.; Juvonen, H.; Arajärvi, R.; Partonen, T.; Suv.

[8129] Further studies establishing the function and utilities of DISC1 are found in John Hopkins OMIM database record ID 605210, and in cited publications numbered 6819–6821, 407 and 6822–6823 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052) is another VGAM74 host target gene.

DSCR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR3 BINDING SITE, designated SEQ ID:12685, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8130] Another function of VGAM74 is therefore inhibition of Down Syndrome Critical Region Gene 3 (DSCR3, Accession NM_006052). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR3. FCRH1 (Accession NM_052938) is another VGAM74 host target gene. FCRH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FCRH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCRH1 BINDING SITE, designated SEQ ID:27499, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8131] Another function of VGAM74 is therefore inhibition of FCRH1 (Accession NM_052938). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCRH1. Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM_022549) is another VGAM74 host target gene. FEZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FEZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEZ1 BINDING SITE, designated SEQ ID:22877, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8132] Another function of VGAM74 is therefore inhibition of Fasciculation and Elongation Protein Zeta 1 (zygin I) (FEZ1, Accession NM_022549), a gene which Zygin 1; may have a role in axonal outgrowth; has similarity to *C. elegans* UNC-76. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEZ1. The function of FEZ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described

hereinabove with reference to VGAM37. Growth Hormone Receptor (GHR, Accession NM_000163) is another VGAM74 host target gene. GHR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GHR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GHR BINDING SITE, designated SEQ ID:5673, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8133] Another function of VGAM74 is therefore inhibition of Growth Hormone Receptor (GHR, Accession NM_000163). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GHR. Mediterranean Fever (MEFV, Accession NM_000243) is another VGAM74 host target gene. MEFV BINDING SITE1 and MEFV BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MEFV, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEFV BINDING SITE1 and

MEFV BINDING SITE2, designated SEQ ID:5769 and SEQ ID:5770 respectively, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8134] Another function of VGAM74 is therefore inhibition of Mediterranean Fever (MEFV, Accession NM_000243). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEFV. Protocadherin Beta 9 (PCDHB9, Accession NM_019119) is another VGAM74 host target gene. PCDHB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHB9 BINDING SITE, designated SEQ ID:21205, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8135] Another function of VGAM74 is therefore inhibition of Protocadherin Beta 9 (PCDHB9, Accession NM_019119), a gene which is a potential calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM74 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHB9. The function of PCDHB9 has been established by previous studies. Cadherins are calcium-dependent cell-cell adhesion molecules that mediate neural cell-cell interactions. Protocadherins constitute a subfamily of nonclassic cadherins. PCDHB9 is a member of the beta cluster of protocadherin genes on 5q31. For specific information on the PCDHB genes, see 604967. Vanhalst et al. (2001) determined that unlike most PCDHB proteins, PCDHB9 has not 1 but 2 PXXP motifs, putative SH3 protein-binding sites, at the end of the conserved region of its cytoplasmic domain.

[8136] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8137] Vanhalst, K.; Kools, P.; Eynde, E. V.; van Roy, F. : The human and murine protocadherin-beta one-exon gene families show high evolutionary conservation, despite the difference in gene number. FEBS Lett. 495: 120-125, 2001. ; and

[8138] Wu, Q.; Zhang, T.; Cheng, J.-F.; Kim, Y.; Grimwood, J.; Schmutz, J.; Dickson, M.; Noonan, J. P.; Zhang, M. Q.; My-

ers, R. M.; Maniatis, T. : Comparative DNA sequence analysis of mouse a.

[8139] Further studies establishing the function and utilities of PCDHB9 are found in John Hopkins OMIM database record ID 606335, and in cited publications numbered 674 and 9535 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphodiesterase 6B, CGMP-specific, Rod, Beta (congenital stationary night blindness 3, autosomal dominant) (PDE6B, Accession NM_000283) is another VGAM74 host target gene. PDE6B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE6B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE6B BINDING SITE, designated SEQ ID:5828, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8140] Another function of VGAM74 is therefore inhibition of Phosphodiesterase 6B, CGMP-specific, Rod, Beta (congenital stationary night blindness 3, autosomal dominant) (PDE6B, Accession NM_000283). Accordingly, utili-

ties of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE6B. Period Homolog 2 (Drosophila) (PER2, Accession NM_022817) is another VGAM74 host target gene. PER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER2 BINDING SITE, designated SEQ ID:23091, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8141] Another function of VGAM74 is therefore inhibition of Period Homolog 2 (Drosophila) (PER2, Accession NM_022817), a gene which Period homolog 2; putative circadian clock protein; has a PAS dimerization domain. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER2. The function of PER2 has been established by previous studies. To investigate the biologic role of NPAS2 (OMIM Ref. No. 603347), Reick et al. (2001) prepared a neuroblastoma cell line capable of conditional induction of the NPAS2:BMAL1 (OMIM Ref. No. 602550)

heterodimer and identified putative target genes by representational difference analysis, DNA microarrays, and Northern blotting. Coinduction of NPAS2 and BMAL1 activated transcription of the endogenous Per1, Per2, and Cry1 (OMIM Ref. No. 601933) genes, which encode negatively activating components of the circadian regulatory apparatus, and repressed transcription of the endogenous BMAL1 gene. Analysis of the frontal cortex of wildtype mice kept in a 24-hour light-dark cycle revealed that Per1, Per2, and Cry1 mRNA levels were elevated during darkness and reduced during light, whereas BMAL1 mRNA displayed the opposite pattern. In situ hybridization assays of mice kept in constant darkness revealed that Per2 mRNA abundance did not oscillate as a function of circadian cycle in NPAS2-deficient mice. Thus, NPAS2 likely functions as part of a molecular clock operative in the mammalian forebrain. Animal model experiments lend further support to the function of PER2. Shearman et al. (2000) demonstrated that in the mouse, the core mechanism for the master circadian clock consists of interacting positive and negative transcription and translation feedback loops. Analysis of Clock/Clock (OMIM Ref. No. 601851) mutant mice, homozygous Per2 mutants, and

Cry-deficient mice revealed substantially altered Bmal1 (OMIM Ref. No. 602550) rhythms, consistent with a dominant role of Per2 in the positive regulation of the Bmal1 loop. In vitro analysis of Cry inhibition of Clock:Bmal1-mediated transcription shows that the inhibition is through direct protein-protein interactions, independent of the Per and Tim (OMIM Ref. No. 603887) proteins. Per2 is a positive regulator of the Bmal1 loop, and Cry1 and Cry2 are the negative regulators of the Period and Cryptochrome cycles.

[8142] It is appreciated that the abovementioned animal model for PER2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8143] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8144] Shearman, L. P.; Sriram, S.; Weaver, D. R.; Maywood, E. S.; Chaves, I.; Zheng, B.; Kume, K.; Lee, C. C.; van der Horst, G. T. J.; Hastings, M. H.; Reppert, S. M. : Interacting molecular loops in the mammalian circadian clock. Science 288: 1013-1019, 2000. ; and

[8145] Shearman, L. P.; Zylka, M. J.; Weaver, D. R.; Kolakowski, L.

F., Jr.; Reppert, S. M. : Two period homologs: circadian expression and photic regulation in the suprachiasmatic nuclei. Neu.

[8146] Further studies establishing the function and utilities of PER2 are found in John Hopkins OMIM database record ID 603426, and in cited publications numbered 933, 957, 6264–6265, 1256, 8191–819 and 8673 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400) is another VGAM74 host target gene. PLA2G2D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G2D BINDING SITE, designated SEQ ID:14767, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8147] Another function of VGAM74 is therefore inhibition of Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400), a gene which is involved in phospholipid digestion, remodeling of cell membranes, and host defense,

as well as pathophysiologic processes. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G2D. The function of PLA2G2D has been established by previous studies. Phospholipase A2 (PLA2) family members (e.g., PLA2G2A; 172411) are lipolytic enzymes that hydrolyze the sn-2 fatty acid ester bond of glycerophospholipids to produce free fatty acid and lysophospholipids. PLA2s are involved in phospholipid digestion, remodeling of cell membranes, and host defense, as well as pathophysiologic processes involving the production of prostaglandins, leukotrienes, thromboxanes, and platelet-activating factor. By searching an EST database using the catalytically essential residues of secretory PLA2s as the probe, followed by PCR of mouse and human spleen cDNA, Ishizaki et al. (1999) obtained cDNAs encoding mouse and human PLA2G2D. Sequence analysis predicted that the 145-amino acid human secretory protein, 48% identical to PLA2G2A, contains a 20-residue signal peptide, a potential N-linked glycosylation site, 14 cysteine residues, and conserved His48 and Asp49 sites. Analysis of enzymatic activity detected most activity in culture supernatant and determined that PLA2G2D preferentially hydrolyzes

phosphatidylglycerol and phosphatidylethanolamine, followed by phosphatidylcholine, but does not hydrolyze phosphatidylserine or phosphatidic acid. Northern blot analysis revealed variable expression of 2.0- and 1.0-kb transcripts, with highest expression in pancreas and spleen. In a rat model, expression in thymus increased dramatically after lipopolysaccharide injection. By subtractive cDNA cloning using spleens from wildtype and tumor necrosis factor (Tnf; 191160)/lymphotoxin-alpha (Lta; 153440) double-knockout mice, followed by probing a spleen cDNA library, Shakhov et al. (2000) isolated a cDNA encoding mouse Pla2g2d, which they designated Splash (secretory-type PLA, stroma-associated homolog). Splash was expressed 6-fold less in mutant than wildtype mice. By screening a human cDNA library, they isolated cDNAs encoding human PLA2G2D. Shakhov et al. (2000) noted that the human and mouse protein sequences are 73% identical and 81% homologous. Northern blot analysis detected mouse Pla2g2d expression in adult but not embryonic spleen. By radiation hybrid mapping, Ishizaki et al. (1999) mapped the PLA2G2D gene to 1p36.12. Also using radiation hybrid analysis, Shakhov et al. (2000) mapped the PLA2G2D gene to 1p36.1-p35, near the PLA2G2A

gene and a region known for frequent loss of heterozygosity in human tumors. Shakhov et al. (2000) mapped the mouse gene to chromosome 4.

[8148] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8149] Ishizaki, J.; Suzuki, N.; Higashino, K.; Yokota, Y.; Ono, T.; Kawamoto, K.; Fujii, N.; Arita, H.; Hanasaki, K. : Cloning and characterization of novel mouse and human secretory phospholipase A(2)s. J. Biol. Chem. 274: 24973–24979, 1999. ; and

[8150] Shakhov, A. N.; Rubtsov, A. V.; Lyakhov, I. G.; Tumanov, A. V.; Nedospasov, S. A. : SPLASH (PLA(2)IID), a novel member of phospholipase A2 family, is associated with lymphotoxin-defici.

[8151] Further studies establishing the function and utilities of PLA2G2D are found in John Hopkins OMIM database record ID 605630, and in cited publications numbered 6963 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rhesus Blood Group, D Antigen (RHD, Accession NM_016124) is another VGAM74 host target gene. RHD BINDING SITE1 and RHD BINDING SITE2 are HOST TARGET binding sites found in

untranslated regions of mRNA encoded by RHD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHD BINDING SITE1 and RHD BINDING SITE2, designated SEQ ID:18217 and SEQ ID:18337 respectively, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8152] Another function of VGAM74 is therefore inhibition of Rhesus Blood Group, D Antigen (RHD, Accession NM_016124), a gene which Major antigen of the RH system. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHD. The function of RHD has been established by previous studies. Bennett et al. (1993) demonstrated that DNA testing can be used to determine RhD type in chorionic villus samples or amniotic cells. An RhD-negative woman whose partner is heterozygous may have preexisting anti-RhD antibodies that may or may not affect a subsequent fetus, depending on whether it is heterozygous. A safe method of determining fetal RhD type early in pregnancy would eliminate the risks to an RhD-negative fetus of fetal blood sampling or serial amniocen-

teses. Levine et al. (1941) showed that hemolytic disease of the fetus occurs in an RhD-positive fetus carried by an RhD-negative woman who has been immunized by transplacental passage of RhD-positive red cells during a previous pregnancy. When the father of the fetus being carried by a sensitized RhD-negative woman is heterozygous for RhD, as more than 50% of people are, half the fetuses will be RhD-negative and therefore require no treatment to avoid erythroblastosis fetalis. The others will be RhD-positive and require sophisticated investigative measures and treatments. Lo et al. (1998) described a noninvasive method of determining fetal RhD status by analyzing maternal plasma. Using a fluorescent-based PCR assay that was sensitive enough to detect the amount of RhD DNA found in a single cell, they determined the RhD status of singleton fetuses from 57 RhD-negative women whose partners were heterozygous for the RhD gene. This method correctly identified the RhD status of 10 of 12 fetuses whose mothers were in their first trimester of pregnancy, that of all 30 fetuses whose mothers were in their second trimester, and that of all 15 fetuses whose mothers were in their third trimester. The method they described was rapid, providing results within 1 day, and rep-

resented a major advance in RhD genotyping.

[8153] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8154] Bennett, P. R.; Le Van Kim, C.; Colin, Y.; Warwick, R. M.; Cherif-Zahar, B.; Fisk, N. M.; Cartron, J.-P. : Prenatal determination of fetal RhD type by DNA amplification. New Eng. J. Med. 329: 607-610, 1993. ; and

[8155] Lo, Y. M. D.; Hjelm, N. M.; Fidler, C.; Sargent, I. L.; Murphy, M. F.; Chamberlain, P. F.; Poon, P. M. K.; Redman, C. W. G.; Wainscoat, J. S. : Prenatal diagnosis of fetal RhD status by mol.

[8156] Further studies establishing the function and utilities of RHD are found in John Hopkins OMIM database record ID 111680, and in cited publications numbered 3747-3776 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Selenoprotein N, 1 (SEPN1, Accession XM_039033) is another VGAM74 host target gene. SEPN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SEPN1 BINDING SITE, designated SEQ ID:32989, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8157] Another function of VGAM74 is therefore inhibition of Selenoprotein N, 1 (SEPN1, Accession XM_039033). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPN1. Solute Carrier Family 13 (sodium/sulfate symporters), Member 1 (SLC13A1, Accession NM_022444) is another VGAM74 host target gene. SLC13A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC13A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC13A1 BINDING SITE, designated SEQ ID:22775, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8158] Another function of VGAM74 is therefore inhibition of Solute Carrier Family 13 (sodium/sulfate symporters), Member 1 (SLC13A1, Accession NM_022444). Accordingly, utilities of VGAM74 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with SLC13A1. Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM_007163) is another VGAM74 host target gene. SLC14A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC14A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC14A2 BINDING SITE, designated SEQ ID:14009, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8159] Another function of VGAM74 is therefore inhibition of Solute Carrier Family 14 (urea transporter), Member 2 (SLC14A2, Accession NM_007163), a gene which is a renal urea transporter 2. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC14A2. The function of SLC14A2 has been established by previous studies. Genetic variation in proteins that determine sodium reabsorption and excretion significantly influences blood pressure. Ranade et al. (2001) investigated whether nucleotide variation in human UT2 could be associated with

variation in blood pressure. Seven single-nucleotide polymorphisms (SNPs) were identified, including val227 to ile and ala357 to thr. Over 1,000 hypertensive and low-normotensive individuals of Chinese origin were genotyped. The ile227 and ala357 alleles were associated with low diastolic blood pressure in men but not women, with odds ratios 2.1 (95% confidence interval 1.5–2.7, P less than 0.001) and 1.5 (95% confidence interval 1.2–1.8, P less than 0.001), respectively. There was a similar trend for systolic blood pressure, and odds ratios for the ile227 and ala357 alleles were 1.7 (95% confidence interval 1.2–2.3, $P = 0.002$) and 1.3 (95% confidence interval 1.1–1.6, $P = 0.007$), respectively, in men. DeStefano et al. (1998) identified a locus for orthostatic hypotension (OHDS; 143850) on chromosome 18q, with a peak lod score of 3.92 at D18S1367 in 2 linked families. The proximity of human UT2 makes it a potential candidate gene for this autosomal dominant disorder.

[8160] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8161] Ranade, K.; Wu, K.-W.; Hwu, C.-M.; Ting, C.-T.; Pei, D.; Pesich, R.; Hebert, J.; Chen, Y.-D. I.; Pratt, R.; Olshen, R.;

Masaki, K.; Risch, N.; Cox, D. R.; Botstein, D. : Genetic variation in the human urea transporter-2 is associated with variation in blood pressure. Hum. Molec. Genet. 10: 2157-2164, 2001. ; and

[8162] DeStefano, A. L.; Baldwin, C. T.; Burzstyn, M.; Gavras, I.; Handy, D. E.; Joost, O.; Martel, T.; Nicolaou, M.; Schwartz, F.; Streeten, D. H. P.; Farrer, L. A.; Gavras, H. : Autosomal domin.

[8163] Further studies establishing the function and utilities of SLC14A2 are found in John Hopkins OMIM database record ID 601611, and in cited publications numbered 12144-9111 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 15 (oligopeptide transporter), Member 1 (SLC15A1, Accession NM_005073) is another VGAM74 host target gene. SLC15A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC15A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC15A1 BINDING SITE, designated SEQ ID:11521, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA,

also designated SEQ ID:2785.

[8164] Another function of VGAM74 is therefore inhibition of Solute Carrier Family 15 (oligopeptide transporter), Member 1 (SLC15A1, Accession NM_005073), a gene which is a H(+)-coupled peptide transporter. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC15A1. The function of SLC15A1 has been established by previous studies. In mammalian small intestine, the proton-coupled peptide transporter is responsible for the absorption of small peptides arising from digestion of dietary proteins. Fei et al. (1994) isolated a cDNA clone encoding a hydrogen ion/peptide cotransporter from a rabbit intestinal cDNA library. Liang et al. (1995) screened a human intestinal cDNA library with a probe derived from the rabbit cotransporter cDNA and identified a cDNA which, when expressed in HeLa cells or in *Xenopus laevis* oocytes, induced proton-dependent peptide transport activity. The predicted protein consisted of 708 amino acids with 12 membrane-spanning domains and 2 putative sites for protein kinase C-dependent phosphorylation. The cDNA-induced transport process accepted dipeptides, tripeptides, and amino beta-lactam antibiotics as sub-

strates, but could not transport free amino acids. The human cotransporter showed 81% identity and 92% similarity to the rabbit cotransporter, but showed only a weak homology to the proton-coupled peptide transport proteins present in bacteria and yeast. By analysis of somatic cell hybrids and by isotopic in situ hybridization, Liang et al. (1995) mapped the human gene to 13q33-q34. Adibi (1997) reviewed the biology and function of the human intestinal oligopeptide transporter, which he symbolized PEPT1. Studies indicated that it transports dipeptides and tripeptides but not free amino acids or peptides with more than 3 amino acid residues and that its driving force for uphill transport requires proton binding and presence of an inside-negative membrane potential. A membrane protein, HTP1, which appeared to be associated with the oligopeptide transporter, had also been cloned. Adibi (1997) pointed out the importance of the transporter in nutritional and pharmacologic therapies; for example, it has allowed the use of oligopeptides as a source of nitrogen for enteral feeding and the use of the oral route for delivery of peptidomimetic drugs such as beta-lactam antibiotics.

[8165] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [8166] Liang, R.; Fei, Y.-J.; Prasad, P. D.; Ramamoorthy, S.; Han, H.; Yang-Feng, T. L.; Hediger, M. A.; Ganapathy, V.; Leibach, F. H. : Human intestinal H(+)/peptide cotransporter: cloning, functional expression, and chromosomal localization. J. Biol. Chem. 270: 6456–6463, 1995. ; and
- [8167] Adibi, S. A. : The oligopeptide transporter (Pept-1) in human intestine: biology and function. Gastroenterology 113: 332–340, 1997.

[8168] Further studies establishing the function and utilities of SLC15A1 are found in John Hopkins OMIM database record ID 600544, and in cited publications numbered 7871–7873 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SMAC (Accession NM_138930) is another VGAM74 host target gene. SMAC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SMAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMAC BINDING SITE, designated SEQ ID:29051, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8169] Another function of VGAM74 is therefore inhibition of SMAC (Accession NM_138930), a gene which promotes apoptosis via caspase activation. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMAC. The function of SMAC has been established by previous studies. Verhagen et al. (2000) identified the murine homolog of SMAC, which they called DIABLO (direct IAP-binding protein with low pI). They showed that DIABLO

can bind mammalian IAP homolog A (MIHA, or API3) and can also interact with MIHB (API1; 601712), MIHC (API2; 601721), and OpiAP, the baculoviral IAP. Immunoprecipitation and Western blot analysis indicated that the N-terminally processed, IAP-interacting form of DIABLO is concentrated in membrane fractions in healthy cells but is released into the MIHA-containing cytosolic fractions upon ultraviolet (UV) irradiation. Since transfection of cells with DIABLO was able to counter the protection afforded by MIHA against UV irradiation, the authors suggested that DIABLO may promote apoptosis by binding to IAPs and preventing them from inhibiting caspases. Chai et al. (2000) showed that SMAC/DIABLO promotes not only the proteolytic activation of procaspase-3, but also the enzymatic activity of mature caspase-3, both of which depend upon its ability to interact physically with IAPs. Animal model experiments lend further support to the function of SMAC. Okada et al. (2002) generated Diablo-deficient mice by homologous recombination. Western blot analysis confirmed the null mutation. The mice were fertile and appeared grossly normal at more than 1 year of age, and histologic analysis failed to detect any abnormalities. In vitro analysis indicated an inhibition of procaspase-3

(CASP3; 600636) cleavage in Diablo $-/-$ cell lysates, but all types of Diablo $-/-$ cells tested responded normally to a number of apoptotic stimuli. Fas (OMIM Ref. No. 134637)-mediated apoptosis in liver was also normal in vivo in these mice. The authors concluded that a redundant molecule, possibly Omi (PRSS25; 606441), or molecules are capable of compensating for the loss of Diablo function. Alternatively, they suggested that Diablo may only regulate programmed cell death in specific situations or tissues not yet identified.

[8170] It is appreciated that the abovementioned animal model for SMAC is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8171] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8172] Okada, H.; Suh, W.-K.; Jin, J.; Woo, M.; Du, C.; Elia, A.; Duncan, G. S.; Wakeham, A.; Itie, A.; Lowe, S. W.; Wang, X.; Mak, T. W. : Generation and characterization of Smac/DIABLO-deficient mice. *Molec. Cell. Biol.* 22: 3509-3517, 2002. ; and

[8173] Verhagen, A. M.; Ekert, P. G.; Pakusch, M.; Silke, J.; Con-

nolly, L. M.; Reid, G. E.; Moritz, R. L.; Simpson, R. J.; Vaux, D. L. : Identification of DIABLO, a mammalian protein that promote.

[8174] Further studies establishing the function and utilities of SMAC are found in John Hopkins OMIM database record ID 605219, and in cited publications numbered 6969–6970, 9213–6972, 921 and 8837 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sorting Nexin 15 (SNX15, Accession XM_057307) is another VGAM74 host target gene. SNX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX15 BINDING SITE, designated SEQ ID:36505, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8175] Another function of VGAM74 is therefore inhibition of Sorting Nexin 15 (SNX15, Accession XM_057307). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX15. Synovial Sarcoma Translocation, Chro-

mosome 18 (SS18, Accession NM_005637) is another VGAM74 host target gene. SS18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SS18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SS18 BINDING SITE, designated SEQ ID:12164, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8176] Another function of VGAM74 is therefore inhibition of Synovial Sarcoma Translocation, Chromosome 18 (SS18, Accession NM_005637), a gene which is a putative transcriptional activator. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SS18. The function of SS18 has been established by previous studies. Human synovial sarcomas contain a recurrent and specific chromosomal translocation t(X;18)(p11.2;q11.2). By screening a synovial sarcoma cDNA library with a YAC spanning the X chromosome breakpoint, Clark et al. (1994) identified a hybrid transcript that contained 5-prime sequences mapping to chromosome 18 and 3-prime sequences mapping

to the X chromosome (see OMIM Ref. No. SSX1; 312820). A probe from the chromosome 18 gene sequence, symbolized SS18, detected genomic rearrangements in 10 of 13 synovial sarcomas. The chromosome 18 gene was symbolized SYT by Clark et al. (1994), but that symbol had already been used for synaptotagmin (OMIM Ref. No. 185605). Sequencing of cDNA clones showed that the normal SS18 gene encodes a protein rich in glutamine, proline, and glycine, and that in synovial sarcoma, rearrangement of the SS18 gene results in the formation of a fusion protein. Both the chromosome 18 and the X chromosome components failed to exhibit significant homology to known gene sequences. The SYT protein appears to act as a transcriptional coactivator and the SSX proteins as corepressors. Thaete et al. (1999) investigated the functional domains of the proteins. The SYT protein was found to contain a novel conserved 54-amino acid domain at the N terminus of the protein (the SNH domain) that is found in proteins from a wide variety of species, and a C-terminal domain, rich in glutamine, proline, glycine, and tyrosine (the QPGY domain), which contains the transcriptional activator sequences. Deletion of the SNH domain resulted in a more active transcriptional activator, sug-

gesting that this domain acts as an inhibitor of the activation domain. The C-terminal SSX domain present in the SYT-SSX translocation protein contributes a transcriptional repressor domain to the protein. Thus, the fusion protein has transcriptional activating and repressing domains. Thaete et al. (1999) demonstrated that the human homolog of the SNF2/Brahma protein BRM (SMARCA2; 600014) colocalizes with SYT and SYT-SSX in nuclear speckles, and also interacts with SYT and SYT-SSX proteins in vitro. They suggested that this interaction may provide an explanation of how the SYT protein activates gene transcription.

[8177] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8178] Clark, J.; Rocques, P. J.; Crew, A. J.; Gill, S.; Shipley, J.; Chan, A. M.-L.; Gusterson, B. A.; Cooper, C. S. : Identification of novel genes, SYT and SSX, involved in the t(X;18)(p11.2;q11.2) translocation found in human synovial sarcoma. *Nature Genet.* 7: 502-508, 1994. ; and

[8179] Thaete, C.; Brett, D.; Monaghan, P.; Whitehouse, S.; Rennie, G.; Rayner, E.; Cooper, C. S.; Goodwin, G. : Functional domains of the SYT and SYT-SSX synovial sarcoma

translocation prote.

[8180] Further studies establishing the function and utilities of SS18 are found in John Hopkins OMIM database record ID 600192, and in cited publications numbered 10626, 11390-10117, 9147-914 and 10118 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite Motif-containing 9 (TRIM9, Accession NM_015163) is another VGAM74 host target gene. TRIM9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRIM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM9 BINDING SITE, designated SEQ ID:17515, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8181] Another function of VGAM74 is therefore inhibition of Tripartite Motif-containing 9 (TRIM9, Accession NM_015163), a gene which may function as a positive regulator for mannosylphosphate transferase and is required to mediate mannosylphosphate transfer in both the core and outer chain portions of n-linked. oligosaccha-

rides. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM9. The function of TRIM9 has been established by previous studies. TRIM proteins are composed of 3 zinc-binding domains, a RING, a B-box type 1, and a B-box type 2, followed by a coiled-coil region. They are involved in development and cell growth. By EST database searching for B-box-containing proteins, Reymond et al. (2001) identified 37 TRIM members, including 3 isoforms of TRIM9. Northern blot analysis revealed high expression of a 4.4-kb TRIM9 transcript in brain. Fluorescence microscopy demonstrated expression of TRIM9 in cytoplasmic speckles. Interaction mating analysis indicated that TRIM9 can form a homodimer.

[8182] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8183] Li, Y.; Chin, L.-S.; Weigel, C.; Li, L. : Spring, a novel RING finger protein that regulates synaptic vesicle exocytosis. *J. Biol. Chem.* 276: 40824–40833, 2001. ; and

[8184] Reymond, A.; Meroni, G.; Fantozzi, A.; Merla, G.; Cairo, S.; Luzi, L.; Riganelli, D.; Zanaria, E.; Messali, S.; Cainarca, S.; Guffanti, A.; Minucci, S.; Pelicci, P. G.; Ballabio, A. .:

[8185] Further studies establishing the function and utilities of TRIM9 are found in John Hopkins OMIM database record ID 606555, and in cited publications numbered 4517–4518 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. UDP–glucose Dehydrogenase (UGDH, Accession NM_003359) is another VGAM74 host target gene. UGDH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UGDH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UGDH BINDING SITE, designated SEQ ID:9388, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8186] Another function of VGAM74 is therefore inhibition of UDP–glucose Dehydrogenase (UGDH, Accession NM_003359), a gene which is an UDP–glucose dehydrogenase. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UGDH. The function of UGDH has been established by previous studies. Spicer et al. (1998) conducted expression studies that indicated that treat–

ment of human fibroblasts with proinflammatory cytokines, such as interleukin-1-beta (OMIM Ref. No. 147720), under conditions that dramatically increase hyaluronan synthesis, also led to a substantial but transient increase in the expression of UGDH. The authors suggested that glycosaminoglycan biosynthesis may be partly regulated by the availability of activated UDP-glucuronate, as determined by relative Udpgdh expression. Animal model experiments lend further support to the function of UGDH. Zebrafish 'jekyll' mutants are deficient in the initiation of heart valve formation. Walsh and Stainier (2001) identified the jekyll mutation as a T-to-A change at basepair 992, resulting in an isoleucine-to-aspartic acid substitution at residue 331 in the zebrafish UDP-glucose dehydrogenase gene. The isoleucine at position 331 is conserved in Drosophila, human, and zebrafish Ugdh and is situated in a pocket of nonpolar amino acids in the 'hinge' of the omega loop gate that allows UDP-glucose access to the active site of the enzyme. While other mutations that affect heparan sulfate proteoglycans in vertebrates result in defects during gastrulation, jekyll exhibits no manifestations until organogenesis. Walsh and Stainier (2001) suggested one explanation

for this incongruity is that zebrafish UdgH mRNA is provided maternally. The atrioventricular border cells do not differentiate from their neighbors in jekyll mutants, suggesting that jekyll is required in a cell signaling event that establishes a boundary between the atrium and the ventricle. Walsh and Stainier (2001) demonstrated that jekyll functions early in the process of atrioventricular valve formation and is required specifically in patterning the myocardium and endocardium at the atrioventricular boundary. The myocardial patterning defects seen in jekyll mutants are likely direct effects of the loss of jekyll function because they are the first molecular defects to be observed, whereas the later endocardial defects may be secondary to the lack of Bmp4 (OMIM Ref. No. 112262) restriction in the myocardium.

[8187] It is appreciated that the abovementioned animal model for UGDH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8188] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8189] Spicer, A. P.; Kaback, L. A.; Smith, T. J.; Seldin, M. F. :

Molecular cloning and characterization of the human and mouse UDP-glucose dehydrogenase genes. J. Biol. Chem. 273: 25117–25124, 1998. ; and

[8190] Walsh, E. C.; Stainier, D. Y. R. : UDP-glucose dehydrogenase required for cardiac valve formation in zebrafish. Science 293: 1670–1674, 2001.

[8191] Further studies establishing the function and utilities of UGDH are found in John Hopkins OMIM database record ID 603370, and in cited publications numbered 8512–8516 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. V–yes–1 Yamaguchi Sarcoma Viral Oncogene Homolog 1 (YES1, Accession NM_005433) is another VGAM74 host target gene. YES1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YES1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YES1 BINDING SITE, designated SEQ ID:11914, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8192] Another function of VGAM74 is therefore inhibition of V–yes–1 Yamaguchi Sarcoma Viral Oncogene Homolog 1

(YES1, Accession NM_005433), a gene which is a putative protein-tyrosine kinase. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YES1. The function of YES1 has been established by previous studies. The YES oncogene is homologous to the gene of the Yamaguchi sarcoma virus. The product of the gene is associated with tyrosine-specific protein kinase activity and its amino acid sequence shows a high degree of homology with that of the SRC gene product of Rous sarcoma virus. Semba et al. (1985) found in DNA from human embryo fibroblasts 10 EcoRI fragments that hybridized with the Yamaguchi sarcoma virus oncogene. Four of these (designated YES1) were assigned to chromosome 18 and 1 (designated YES2) was assigned to chromosome 6 by a study of human-mouse cell hybrids. (YES2 was later found (Semba et al., 1988) to be a pseudogene of YES1 and to be located at 22q11.2. Semba et al. (1988) stated: 'The failure of proper mapping in our earlier experiment might have been caused by instability of hybrid cell clones.') The other 5 fragments could not be mapped either because hybridization signals were too weak or differentiation from mouse YES fragments was impossible. There was evidence for

multiple copies of YES-related genes in the human genome, but only a single RNA species, 4.8 kb long, was found. At least 3 of the human YES gene copies had both introns and exons and 1 gene copy appeared to be a pseudogene. By isotopic in situ hybridization, Yoshida et al. (1985) mapped the YES1 gene to 18q21.3. These workers suggested that the localization is consistent with a role in the pathogenesis of follicular lymphoma, which is frequently associated with a 14;18 translocation with the breakpoint at 18q21 (Fukuhara et al., 1979); see 151430. Ohno et al. (1987) found that although it is in the same chromosome region as BCL2 (OMIM Ref. No. 151430), the YES gene is intact in cases of follicular lymphoma. Using yeast artificial chromosomes (YACs) containing the YES1 gene as probes and fluorescence in situ hybridization, Silverman et al. (1993) detected a strong signal in the region corresponding to 18p11.3. These YACs were found to contain another 18p11.32 gene, thymidylate synthase (OMIM Ref. No. 188350); the genes were less than 50 kb apart. Overhauser et al. (1993) identified a sequence tagged site (STS) in the YES1 gene and used it in studies of somatic cell hybrids with deletion of various segments of chromosome 18 to map the gene to 18pter-p11.21.

- [8193] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8194] Semba, K.; Yamanashi, Y.; Nishizawa, M.; Sukegawa, J.; Yoshida, M.; Sasaki, M.; Yamamoto, T.; Toyoshima, K. : Location of the c-yes gene on the human chromosome and its expression in various tissues. Science 227: 1038–1040, 1985. ; and
- [8195] Overhauser, J.; Mewar, R.; Rojas, K.; Lia, K.; Kline, A. D.; Silverman, G. A. : STS map of genes and anonymous DNA fragments on human chromosome 18 using a panel of somatic cell hybrids.
- [8196] Further studies establishing the function and utilities of YES1 are found in John Hopkins OMIM database record ID 164880, and in cited publications numbered 3148–3149, 11918–315 and 1694 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926) is another VGAM74 host target gene. ZFP36L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP36L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of ZFP36L1 BINDING SITE, designated SEQ ID:11362, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8197] Another function of VGAM74 is therefore inhibition of Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926), a gene which is a regulatory protein involved in regulating the response to growth factors. Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP36L1. The function of ZFP36L1 has been established by previous studies. Bustin et al. (1994) cloned and characterized the ZFP36L1 gene, which they called ERF1, which is a member of the Tis11 family of early-response genes (see OMIM Ref. No. ZFP36; 190700). Members of this gene family contain a distinguishing putative zinc finger domain with a repeating cys-his motif and are induced by various agonists such as the phorbol ester TPA and the polypeptide mitogen EGF (OMIM Ref. No. 131530). The human gene was cloned using a rat homolog as a probe. The rat and human genes have conserved 5-prime and 3-prime UTRs and their promoters

contain motifs seen in other early-response genes. The predicted rat and human proteins are 99% identical. Bustin et al. (1994) determined that the ZFP36L1 gene contains 2 exons and spans about 6 kb of genomic DNA including the promoter and UTRs. Ning et al. (1996) also cloned ZFP36L1, which they termed BERG36 (B-cell early response gene encoding a 36-kD protein). The deduced 338-amino acid BERG36 protein could be induced by treatment with calcium ionophore, and the induction could be blocked by treatment with interleukin-4 (IL4; 147780) but not by CD40 (TNFRSF5; 109535) ligation. Treatment of the Epstein-Barr virus-negative human Burkitt lymphoma cell line Ramos, which phenotypically resembles germinal center B cells, with BERG36-antisense or with IL4 or CD40 ligation protected the cells from ionophore-induced apoptosis. CD40 ligation also protected Ramos cells from apoptosis induced by inhibitors of macromolecular synthesis. Ning et al. (1996) concluded that BERG36 is a target of IL4 signaling for B-cell survival.

[8198] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8199] Bustin, S. A.; Xiao-Feng, N.; Barnard, R. C.; Kumar, V.;

Pascall, J. C.; Brown, K. D.; Leigh, I. M.; Williams, N. S.; McKay, I. A. : Cloning and characterisation of ERF1, a human member of the Tis11 family of early-response genes. DNA Cell Biol. 13: 449-459, 1994. ; and

[8200] Ning, Z.-Q.; Norton, J. D.; Li, J.; Murphy, J. J. : Distinct mechanisms for rescue from apoptosis in Ramos human B cells by signaling through CD40 and interleukin-4 receptor: a role for.

[8201] Further studies establishing the function and utilities of ZFP36L1 are found in John Hopkins OMIM database record ID 601064, and in cited publications numbered 7811-7814 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BCL2-associated Athanogene 5 (BAG5, Accession NM_004873) is another VGAM74 host target gene. BAG5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG5 BINDING SITE, designated SEQ ID:11303, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8202] Another function of VGAM74 is therefore inhibition of BCL2-associated Athanogene 5 (BAG5, Accession NM_004873). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG5. Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956) is another VGAM74 host target gene. C9orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C9orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf9 BINDING SITE, designated SEQ ID:21028, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8203] Another function of VGAM74 is therefore inhibition of Chromosome 9 Open Reading Frame 9 (C9orf9, Accession NM_018956). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf9. Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444) is another VGAM74 host target gene. CHRAC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CHRAC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRAC1 BINDING SITE, designated SEQ ID:18904, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8204] Another function of VGAM74 is therefore inhibition of Chromatin Accessibility Complex 1 (CHRAC1, Accession NM_017444). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRAC1. DKFZP564I122 (Accession XM_032397) is another VGAM74 host target gene. DKFZP564I122 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I122, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I122 BINDING SITE, designated SEQ ID:31644, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8205] Another function of VGAM74 is therefore inhibition of DK-

FZP564I122 (Accession XM_032397). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DK-FZP564I122. FLJ00024 (Accession XM_033361) is another VGAM74 host target gene. FLJ00024 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ00024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00024 BINDING SITE, designated SEQ ID:31892, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8206] Another function of VGAM74 is therefore inhibition of FLJ00024 (Accession XM_033361). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00024. FLJ10346 (Accession NM_018065) is another VGAM74 host target gene. FLJ10346 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ10346 BINDING SITE, designated SEQ ID:19837, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8207] Another function of VGAM74 is therefore inhibition of FLJ10346 (Accession NM_018065). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10346. FLJ10535 (Accession NM_018129) is another VGAM74 host target gene. FLJ10535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10535 BINDING SITE, designated SEQ ID:19919, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8208] Another function of VGAM74 is therefore inhibition of FLJ10535 (Accession NM_018129). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10535. FLJ10846 (Accession NM_018241) is another VGAM74

host target gene. FLJ10846 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10846 BINDING SITE, designated SEQ ID:20199, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8209] Another function of VGAM74 is therefore inhibition of FLJ10846 (Accession NM_018241). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10846. FLJ12572 (Accession NM_022905) is another VGAM74 host target gene. FLJ12572 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23198, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8210] Another function of VGAM74 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. FLJ14950 (Accession NM_032865) is another VGAM74 host target gene. FLJ14950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14950 BINDING SITE, designated SEQ ID:26673, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8211] Another function of VGAM74 is therefore inhibition of FLJ14950 (Accession NM_032865). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14950. FLJ22002 (Accession NM_024838) is another VGAM74 host target gene. FLJ22002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22002 BINDING SITE, designated SEQ ID:24246, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8212] Another function of VGAM74 is therefore inhibition of FLJ22002 (Accession NM_024838). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22002. FLJ22531 (Accession NM_024650) is another VGAM74 host target gene. FLJ22531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22531 BINDING SITE, designated SEQ ID:23945, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8213] Another function of VGAM74 is therefore inhibition of FLJ22531 (Accession NM_024650). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22531.

FLJ22794 (Accession XM_166220) is another VGAM74 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE, designated SEQ ID:44028, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8214] Another function of VGAM74 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. FLJ23053 (Accession NM_022907) is another VGAM74 host target gene. FLJ23053 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23053, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23053 BINDING SITE, designated SEQ ID:23206, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2785.

[8215] Another function of VGAM74 is therefore inhibition of FLJ23053 (Accession NM_022907). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23053. FLJ23392 (Accession NM_024784) is another VGAM74 host target gene. FLJ23392 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23392, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23392 BINDING SITE, designated SEQ ID:24161, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8216] Another function of VGAM74 is therefore inhibition of FLJ23392 (Accession NM_024784). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23392. FLJ23519 (Accession NM_032240) is another VGAM74 host target gene. FLJ23519 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23519, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23519 BINDING SITE, designated SEQ ID:25976, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8217] Another function of VGAM74 is therefore inhibition of FLJ23519 (Accession NM_032240). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23519. FLJ23563 (Accession XM_041701) is another VGAM74 host target gene. FLJ23563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23563 BINDING SITE, designated SEQ ID:33563, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8218] Another function of VGAM74 is therefore inhibition of FLJ23563 (Accession XM_041701). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ23563. FLJ25416 (Accession NM_145018) is another VGAM74 host target gene. FLJ25416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ25416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ25416 BINDING SITE, designated SEQ ID:29625, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8219] Another function of VGAM74 is therefore inhibition of FLJ25416 (Accession NM_145018). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ25416. GAL3ST-4 (Accession NM_024637) is another VGAM74 host target gene. GAL3ST-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GAL3ST-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAL3ST-4 BINDING SITE, designated SEQ ID:23911, to the nucleotide se-

quence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8220] Another function of VGAM74 is therefore inhibition of GAL3ST-4 (Accession NM_024637). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAL3ST-4. Golgi Autoantigen, Golgin Subfamily A, 3 (GOLGA3, Accession NM_005895) is another VGAM74 host target gene. GOLGA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA3 BINDING SITE, designated SEQ ID:12514, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8221] Another function of VGAM74 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 3 (GOLGA3, Accession NM_005895). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA3. H-plk (Accession NM_015852) is another VGAM74 host target

gene. H-plk BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by H-plk, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H-plk BINDING SITE, designated SEQ ID:17985, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8222] Another function of VGAM74 is therefore inhibition of H-plk (Accession NM_015852). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H-plk. KIAA0426 (Accession NM_014724) is another VGAM74 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16310, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8223] Another function of VGAM74 is therefore inhibition of

KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA0469 (Accession NM_014851) is another VGAM74 host target gene. KIAA0469 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0469 BINDING SITE, designated SEQ ID:16891, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8224] Another function of VGAM74 is therefore inhibition of KIAA0469 (Accession NM_014851). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0469. KIAA0527 (Accession XM_171054) is another VGAM74 host target gene. KIAA0527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0527 BINDING SITE, designated SEQ ID:45846, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8225] Another function of VGAM74 is therefore inhibition of KIAA0527 (Accession XM_171054). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0527. KIAA0561 (Accession XM_038150) is another VGAM74 host target gene. KIAA0561 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0561, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0561 BINDING SITE, designated SEQ ID:32764, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8226] Another function of VGAM74 is therefore inhibition of KIAA0561 (Accession XM_038150). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0561. KIAA0599 (Accession XM_085127) is another

VGAM74 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37856, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8227] Another function of VGAM74 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA0841 (Accession XM_049237) is another VGAM74 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35361, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8228] Another function of VGAM74 is therefore inhibition of KIAA0841 (Accession XM_049237). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0841. KIAA1054 (Accession XM_043493) is another VGAM74 host target gene. KIAA1054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1054 BINDING SITE, designated SEQ ID:33953, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8229] Another function of VGAM74 is therefore inhibition of KIAA1054 (Accession XM_043493). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1054. KIAA1198 (Accession XM_032674) is another VGAM74 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31708, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8230] Another function of VGAM74 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1373 (Accession XM_048195) is another VGAM74 host target gene. KIAA1373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1373 BINDING SITE, designated SEQ ID:35127, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8231] Another function of VGAM74 is therefore inhibition of KIAA1373 (Accession XM_048195). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1373. KIAA1443 (Accession XM_033392) is another VGAM74 host target gene. KIAA1443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1443 BINDING SITE, designated SEQ ID:31931, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8232] Another function of VGAM74 is therefore inhibition of KIAA1443 (Accession XM_033392). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1443. KIAA1497 (Accession XM_041431) is another VGAM74 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33528, to the nucleotide sequence of VGAM74 RNA, herein designated

VGAM RNA, also designated SEQ ID:2785.

[8233] Another function of VGAM74 is therefore inhibition of KIAA1497 (Accession XM_041431). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1497. KIAA1615 (Accession XM_044021) is another VGAM74 host target gene. KIAA1615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1615 BINDING SITE, designated SEQ ID:34084, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8234] Another function of VGAM74 is therefore inhibition of KIAA1615 (Accession XM_044021). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1615. KIAA1922 (Accession XM_057040) is another VGAM74 host target gene. KIAA1922 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1922, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1922 BINDING SITE, designated SEQ ID:36455, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8235] Another function of VGAM74 is therefore inhibition of KIAA1922 (Accession XM_057040). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1922. KIAA1924 (Accession XM_057091) is another VGAM74 host target gene. KIAA1924 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1924 BINDING SITE, designated SEQ ID:36475, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8236] Another function of VGAM74 is therefore inhibition of KIAA1924 (Accession XM_057091). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1924. KIAA1971 (Accession XM_058720) is another VGAM74 host target gene. KIAA1971 BINDING SITE1 and KIAA1971 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1971, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1971 BINDING SITE1 and KIAA1971 BINDING SITE2, designated SEQ ID:36729 and SEQ ID:36730 respectively, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8237] Another function of VGAM74 is therefore inhibition of KIAA1971 (Accession XM_058720). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1971. Lymphocyte Antigen 75 (LY75, Accession NM_002349) is another VGAM74 host target gene. LY75 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LY75, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LY75 BINDING SITE, designated SEQ ID:8148, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8238] Another function of VGAM74 is therefore inhibition of Lymphocyte Antigen 75 (LY75, Accession NM_002349). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LY75. Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379) is another VGAM74 host target gene. MAN1C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1C1 BINDING SITE, designated SEQ ID:21645, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8239] Another function of VGAM74 is therefore inhibition of Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with MAN1C1. MCLC (Accession NM_015127) is another VGAM74 host target gene. MCLC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MCLC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MCLC BINDING SITE, designated SEQ ID:17491, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8240] Another function of VGAM74 is therefore inhibition of MCLC (Accession NM_015127). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MCLC. MGC11115 (Accession NM_032310) is another VGAM74 host target gene. MGC11115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11115 BINDING SITE, designated SEQ ID:26091, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA,

also designated SEQ ID:2785.

[8241] Another function of VGAM74 is therefore inhibition of MGC11115 (Accession NM_032310). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11115. MGC15631 (Accession NM_032753) is another VGAM74 host target gene. MGC15631 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15631, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15631 BINDING SITE, designated SEQ ID:26489, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8242] Another function of VGAM74 is therefore inhibition of MGC15631 (Accession NM_032753). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15631. MGC35558 (Accession NM_145013) is another VGAM74 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29611, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8243] Another function of VGAM74 is therefore inhibition of MGC35558 (Accession NM_145013). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. MGC5149 (Accession XM_051200) is another VGAM74 host target gene. MGC5149 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC5149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5149 BINDING SITE, designated SEQ ID:35784, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8244] Another function of VGAM74 is therefore inhibition of MGC5149 (Accession XM_051200). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC5149. moblak (Accession NM_130807) is another VGAM74 host target gene. moblak BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by moblak, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of moblak BINDING SITE, designated SEQ ID:28308, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8245] Another function of VGAM74 is therefore inhibition of moblak (Accession NM_130807). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with moblak. Molybdenum Cofactor Synthesis 3 (MOCS3, Accession NM_014484) is another VGAM74 host target gene. MOCS3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MOCS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOCS3 BINDING SITE, designated SEQ ID:15830, to the

nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8246] Another function of VGAM74 is therefore inhibition of Molybdenum Cofactor Synthesis 3 (MOCS3, Accession NM_014484). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOCS3. Phosphoserine Phosphatase (PSPH, Accession NM_004577) is another VGAM74 host target gene. PSPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSPH BINDING SITE, designated SEQ ID:10924, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8247] Another function of VGAM74 is therefore inhibition of Phosphoserine Phosphatase (PSPH, Accession NM_004577). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSPH. RAB21, Member RAS Oncogene Family (RAB21, Accession NM_014999) is an-

other VGAM74 host target gene. RAB21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB21 BINDING SITE, designated SEQ ID:17367, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8248] Another function of VGAM74 is therefore inhibition of RAB21, Member RAS Oncogene Family (RAB21, Accession NM_014999). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB21. RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM_031296) is another VGAM74 host target gene. RAB33B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB33B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB33B BINDING SITE, designated SEQ ID:25329, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA,

also designated SEQ ID:2785.

[8249] Another function of VGAM74 is therefore inhibition of RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM_031296). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB33B. RAP140 (Accession NM_015224) is another VGAM74 host target gene. RAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAP140 BINDING SITE, designated SEQ ID:17557, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8250] Another function of VGAM74 is therefore inhibition of RAP140 (Accession NM_015224). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAP140. RNF9 (Accession NM_052828) is another VGAM74 host target gene. RNF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by RNF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF9 BINDING SITE, designated SEQ ID:27409, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8251] Another function of VGAM74 is therefore inhibition of RNF9 (Accession NM_052828). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF9. STAF65(gamma) (Accession NM_014860) is another VGAM74 host target gene. STAF65(gamma) BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAF65(gamma), corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAF65(gamma) BINDING SITE, designated SEQ ID:16924, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8252] Another function of VGAM74 is therefore inhibition of STAF65(gamma) (Accession NM_014860). Accordingly,

utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAF65(gamma). Synaptotagmin XIII (SYT13, Accession XM_167880) is another VGAM74 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44889, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8253] Another function of VGAM74 is therefore inhibition of Synaptotagmin XIII (SYT13, Accession XM_167880). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. TADA3L (Accession NM_133480) is another VGAM74 host target gene. TADA3L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TADA3L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TADA3L BINDING SITE, designated SEQ ID:28547, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8254] Another function of VGAM74 is therefore inhibition of TADA3L (Accession NM_133480). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TADA3L. UBF-fl (Accession NM_032828) is another VGAM74 host target gene. UBF-fl BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBF-fl, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBF-fl BINDING SITE, designated SEQ ID:26602, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8255] Another function of VGAM74 is therefore inhibition of UBF-fl (Accession NM_032828). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBF-fl. LOC126661 (Accession XM_059061) is another VGAM74

host target gene. LOC126661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126661 BINDING SITE, designated SEQ ID:36851, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8256] Another function of VGAM74 is therefore inhibition of LOC126661 (Accession XM_059061). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126661. LOC128989 (Accession XM_059310) is another VGAM74 host target gene. LOC128989 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC128989, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC128989 BINDING SITE, designated SEQ ID:36943, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8257] Another function of VGAM74 is therefore inhibition of LOC128989 (Accession XM_059310). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC128989. LOC135293 (Accession XM_072402) is another VGAM74 host target gene. LOC135293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135293 BINDING SITE, designated SEQ ID:37493, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8258] Another function of VGAM74 is therefore inhibition of LOC135293 (Accession XM_072402). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135293. LOC146784 (Accession XM_085588) is another VGAM74 host target gene. LOC146784 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146784, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146784 BINDING SITE, designated SEQ ID:38238, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8259] Another function of VGAM74 is therefore inhibition of LOC146784 (Accession XM_085588). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146784. LOC146909 (Accession XM_085634) is another VGAM74 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38266, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8260] Another function of VGAM74 is therefore inhibition of LOC146909 (Accession XM_085634). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146909. LOC146952 (Accession XM_097138) is another VGAM74 host target gene. LOC146952 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146952, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146952 BINDING SITE, designated SEQ ID:40767, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8261] Another function of VGAM74 is therefore inhibition of LOC146952 (Accession XM_097138). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146952. LOC147071 (Accession XM_054031) is another VGAM74 host target gene. LOC147071 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147071 BINDING SITE, designated SEQ ID:36136, to the nucleotide sequence of VGAM74 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2785.

[8262] Another function of VGAM74 is therefore inhibition of LOC147071 (Accession XM_054031). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147071. LOC147694 (Accession XM_085843) is another VGAM74 host target gene. LOC147694 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147694 BINDING SITE, designated SEQ ID:38372, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8263] Another function of VGAM74 is therefore inhibition of LOC147694 (Accession XM_085843). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147694. LOC147817 (Accession XM_085903) is another VGAM74 host target gene. LOC147817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147817, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147817 BINDING SITE, designated SEQ ID:38385, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8264] Another function of VGAM74 is therefore inhibition of LOC147817 (Accession XM_085903). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147817. LOC149821 (Accession XM_097751) is another VGAM74 host target gene. LOC149821 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149821 BINDING SITE, designated SEQ ID:41109, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8265] Another function of VGAM74 is therefore inhibition of LOC149821 (Accession XM_097751). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC149821. LOC151475 (Accession XM_098063) is another VGAM74 host target gene. LOC151475 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151475 BINDING SITE, designated SEQ ID:41356, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8266] Another function of VGAM74 is therefore inhibition of LOC151475 (Accession XM_098063). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151475. LOC152300 (Accession XM_087432) is another VGAM74 host target gene. LOC152300 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152300 BINDING SITE, designated SEQ ID:39251, to

the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8267] Another function of VGAM74 is therefore inhibition of LOC152300 (Accession XM_087432). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152300. LOC152794 (Accession XM_087525) is another VGAM74 host target gene. LOC152794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152794 BINDING SITE, designated SEQ ID:39320, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8268] Another function of VGAM74 is therefore inhibition of LOC152794 (Accession XM_087525). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152794. LOC153579 (Accession XM_087714) is another VGAM74 host target gene. LOC153579 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC153579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153579 BINDING SITE, designated SEQ ID:39404, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8269] Another function of VGAM74 is therefore inhibition of LOC153579 (Accession XM_087714). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153579. LOC153811 (Accession XM_087779) is another VGAM74 host target gene. LOC153811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153811 BINDING SITE, designated SEQ ID:39416, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8270] Another function of VGAM74 is therefore inhibition of LOC153811 (Accession XM_087779). Accordingly, utilities

of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153811. LOC154282 (Accession XM_098505) is another VGAM74 host target gene. LOC154282 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC154282, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154282 BINDING SITE, designated SEQ ID:41699, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8271] Another function of VGAM74 is therefore inhibition of LOC154282 (Accession XM_098505). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154282. LOC157798 (Accession XM_098827) is another VGAM74 host target gene. LOC157798 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC157798 BINDING SITE, designated SEQ ID:41848, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8272] Another function of VGAM74 is therefore inhibition of LOC157798 (Accession XM_098827). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157798. LOC196047 (Accession XM_116883) is another VGAM74 host target gene. LOC196047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196047 BINDING SITE, designated SEQ ID:43144, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8273] Another function of VGAM74 is therefore inhibition of LOC196047 (Accession XM_116883). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196047. LOC200339 (Accession XM_117226) is another VGAM74 host target gene. LOC200339 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC200339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200339 BINDING SITE, designated SEQ ID:43298, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8274] Another function of VGAM74 is therefore inhibition of LOC200339 (Accession XM_117226). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200339. LOC200860 (Accession XM_117289) is another VGAM74 host target gene. LOC200860 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC200860, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200860 BINDING SITE, designated SEQ ID:43354, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8275] Another function of VGAM74 is therefore inhibition of

LOC200860 (Accession XM_117289). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200860. LOC201173 (Accession XM_113312) is another VGAM74 host target gene. LOC201173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201173 BINDING SITE, designated SEQ ID:42215, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8276] Another function of VGAM74 is therefore inhibition of LOC201173 (Accession XM_113312). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201173. LOC201220 (Accession XM_113321) is another VGAM74 host target gene. LOC201220 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC201220 BINDING SITE, designated SEQ ID:42222, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8277] Another function of VGAM74 is therefore inhibition of LOC201220 (Accession XM_113321). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201220. LOC201411 (Accession XM_031946) is another VGAM74 host target gene. LOC201411 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201411 BINDING SITE, designated SEQ ID:31528, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8278] Another function of VGAM74 is therefore inhibition of LOC201411 (Accession XM_031946). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201411. LOC202025 (Accession XM_117353) is an-

other VGAM74 host target gene. LOC202025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202025 BINDING SITE, designated SEQ ID:43402, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8279] Another function of VGAM74 is therefore inhibition of LOC202025 (Accession XM_117353). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202025. LOC203297 (Accession XM_059986) is another VGAM74 host target gene. LOC203297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203297 BINDING SITE, designated SEQ ID:37136, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8280] Another function of VGAM74 is therefore inhibition of LOC203297 (Accession XM_059986). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203297. LOC203350 (Accession XM_117536) is another VGAM74 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43534, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8281] Another function of VGAM74 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC219735 (Accession XM_167601) is another VGAM74 host target gene. LOC219735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219735, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219735 BINDING SITE, designated SEQ ID:44720, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8282] Another function of VGAM74 is therefore inhibition of LOC219735 (Accession XM_167601). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219735. LOC221463 (Accession XM_166374) is another VGAM74 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44203, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8283] Another function of VGAM74 is therefore inhibition of LOC221463 (Accession XM_166374). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221463. LOC222070 (Accession XM_168433) is another VGAM74 host target gene. LOC222070 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222070 BINDING SITE, designated SEQ ID:45181, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8284] Another function of VGAM74 is therefore inhibition of LOC222070 (Accession XM_168433). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222070. LOC253666 (Accession XM_170799) is another VGAM74 host target gene. LOC253666 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253666 BINDING SITE, designated SEQ ID:45568, to the nucleotide sequence of VGAM74 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2785.

[8285] Another function of VGAM74 is therefore inhibition of LOC253666 (Accession XM_170799). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253666. LOC256360 (Accession XM_172918) is another VGAM74 host target gene. LOC256360 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256360 BINDING SITE, designated SEQ ID:46175, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8286] Another function of VGAM74 is therefore inhibition of LOC256360 (Accession XM_172918). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256360. LOC90371 (Accession XM_031261) is another VGAM74 host target gene. LOC90371 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90371, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90371 BINDING SITE, designated SEQ ID:31321, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8287] Another function of VGAM74 is therefore inhibition of LOC90371 (Accession XM_031261). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90371. LOC91115 (Accession XM_036218) is another VGAM74 host target gene. LOC91115 BINDING SITE1 and LOC91115 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91115, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91115 BINDING SITE1 and LOC91115 BINDING SITE2, designated SEQ ID:32396 and SEQ ID:32395 respectively, to the nucleotide sequence of VGAM74 RNA, herein designated VGAM RNA, also designated SEQ ID:2785.

[8288] Another function of VGAM74 is therefore inhibition of

LOC91115 (Accession XM_036218). Accordingly, utilities of VGAM74 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91115. CD164 Antigen, Sialomucin (CD164, Accession NM_006016) is another VGAM75 host target gene. CD164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD164 BINDING SITE, designated SEQ ID:12631, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8289] Another function of VGAM75 is therefore inhibition of CD164 Antigen, Sialomucin (CD164, Accession NM_006016), a gene which plays a role in hematopoiesis by facilitating the adhesion of CD34+ cells to bone marrow stroma and negatively regulates CD34+ hematopoietic progenitor cell growth. Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD164. The function of CD164 has been established by previous

studies. The sialomucins appear to play 2 key but opposing roles in vivo: the first as cytoprotective or antiadhesive agents, and the second as adhesion receptors. Despite their common functions, these mucins encompass a heterogeneous group of secreted or membrane-associated proteins. Using 2 monoclonal antibodies and a retroviral expression cloning strategy, Zannettino et al. (1998) isolated a cDNA encoding a novel transmembrane isoform of the mucin-like glycoprotein MGC-24, which they designated CD164. The mature CD164 protein contains 178 amino acids, has a molecular mass of 80 to 90 kD, and is extremely rich in serine and threonine. CD164 is expressed by human CD34+ (OMIM Ref. No. 142230) hematopoietic progenitor cells. Zannettino et al. (1998) found that the CD164 receptor appears to play a role in hematopoiesis by facilitating the adhesion of CD34+ cells to bone marrow stroma and by negatively regulating CD34+ hematopoietic progenitor cell growth. They found that these functional effects are mediated by at least 2 spatially distinct epitopes, defined by specific monoclonal antibodies. Watt et al. (1998) showed that these and other CD164 monoclonal antibodies show distinct patterns of reactivity when analyzed on hematopoietic cells from nor-

mal human bone marrow, umbilical cord blood, and peripheral blood. Expression of the CD164 epitope was found on developing myelomonocytic cells in bone marrow, being downregulated on mature neutrophils but maintained on monocytes in the peripheral blood. Watt et al. (1998) extended these studies further to identify PAC clones containing the CD164 gene and used the clone to localize the CD164 gene specifically to 6q21 by fluorescence in situ hybridization.

[8290] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8291] Watt, S. M.; Buhring, H.-J.; Rappold, I.; Chan, J. Y.-H.; Lee-Prudhoe, J.; Jones, T.; Zannettino, A. C. W.; Simmons, P. J.; Doyonnas, R.; Sheer, D.; Butler, L. H. : CD164, a novel sialomucin on CD34+ and erythroid subsets, is located on human chromosome 6q21. Blood 92: 849-866, 1998. ; and

[8292] Zannettino, A. C. W.; Buhring, H.-J.; Niutta, S.; Watt, S. M.; Benton, M. A.; Simmons, P. J. : The sialomucin CD164 (MGC-24v) is an adhesive glycoprotein expressed by human hematopoietic.

[8293] Further studies establishing the function and utilities of

CD164 are found in John Hopkins OMIM database record ID 603356, and in cited publications numbered 1090–1091 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PCTAIRE Protein Kinase 1 (PCTK1, Accession NM_033018) is another VGAM75 host target gene. PCTK1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PCTK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTK1 BINDING SITE, designated SEQ ID:26909, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8294] Another function of VGAM75 is therefore inhibition of PCTAIRE Protein Kinase 1 (PCTK1, Accession NM_033018), a gene which may play a role in signal transduction cascades in terminally differentiated cells. Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCTK1. The function of PCTK1 has been established by previous studies. The mechanisms that govern the progression through the eukaryotic cell cycle consist of mul-

multiple regulatory processes that control discrete transition points, such as the G₀/G₁ and G₁/S transitions and the entry into mitosis. One of the key components regulating the initiation and passage through mitosis is the serine/threonine-specific protein kinase, p34(cdc2/CDC28); see 116953. There exists an extended gene family encoding a large number of different cdc2-related serine/threonine-specific protein kinases. The PCTAIRE protein kinases comprise a distinct subfamily of these kinases and are so named for the presence of a cysteine-for-serine substitution in the conserved PSTAIRE amino acid motif found in prototypic cdc2 kinases. Three members of this kinase subfamily, PCTAIRE 1–3, were identified in humans (Meyerson et al., 1992), whereas only 2 members were identified in mice, PCTAIRE1 and –3 (Okuda et al., 1992). The 3 PCTAIRE kinases are 65% identical to one another (80% within the catalytic domain). PCTAIRE1 is ubiquitously expressed with the highest levels detected in the brain and testis. Human PCTAIRE cDNAs do not complement yeast cdc28 mutants and show other differences, suggesting that PCTAIRE kinases have different cellular functions from those described for CDC2 (OMIM Ref. No. 116940). By screening a human genomic library with

murine PCTAIRE cDNA probes, Okuda et al. (1994) isolated human cosmid clones for the PCTK1 and PCTK3 genes. Using these as probes for fluorescence in situ hybridization analyses, they showed that PCTK1 and PCTK3 are located on bands Xp11 and 1q31-q32, respectively. Knight et al. (1995) found that PCTK1 maps distal to the t(X;18) synovial sarcoma breakpoint in Xp11.23. A 420-kb YAC clone positive for PCTK1 also contained the gene coding for ubiquitin-activating enzyme UBE1 (OMIM Ref. No. 314370), previously mapped to Xp11.3.

- [8295] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8296] Okuda, T.; Cleveland, J. L.; Downing, J. R. : PCTAIRE-1 and PCTAIRE-3, two members of a novel cdc2/CDC28-related protein kinase gene family. *Oncogene* 7: 2249-2258, 1992. ; and
- [8297] Okuda, T.; Valentine, V. A.; Shapiro, D. N.; Downing, J. R. : Cloning of genomic loci and chromosomal localization of the human PCTAIRE-1 and -3 protein kinase genes. *Genomics* 21: 217-22.
- [8298] Further studies establishing the function and utilities of PCTK1 are found in John Hopkins OMIM database record

ID 311550, and in cited publications numbered 1064 and 3501–3502 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Reversion-inducing-cysteine-rich Protein with Kazal Motifs (RECK, Accession NM_021111) is another VGAM75 host target gene. RECK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RECK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RECK BINDING SITE, designated SEQ ID:22090, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8299] Another function of VGAM75 is therefore inhibition of Reversion-inducing-cysteine-rich Protein with Kazal Motifs (RECK, Accession NM_021111), a gene which plays a role in regulation of cancer progression and tumor angiogenesis. Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RECK. The function of RECK has been established by previous studies. Transformed malignant cell lines frequently lose a flat morphology and ac-

quire a round morphology. Genes that induce flat reversion may be useful in the control of cancer. By screening a fibroblast expression library for reversion-inducing cDNAs, Takahashi et al. (1998) isolated a cDNA encoding RECK (reversion-inducing, cysteine-rich protein with Kazal motifs). Sequence analysis predicted that the 971-amino acid RECK protein, which shares 93% amino acid identity with mouse Reck, is 9% cysteine and contains an N-terminal signal sequence; 5 putative cysteine knot motifs; 5 potential N-glycosylation sites; 3 central serine protease inhibitor domains with either complete or incomplete Kazal-type, 4-cys motifs; 2 regions with weak homology to EGF-like repeats; and a C-terminal hydrophobic glycosylphosphatidylinositol-anchoring signal. Immunoblot analysis showed that RECK is expressed as a 110-kD protein that is reduced to approximately 100 kD after deglycosylation. Northern blot analysis detected a 4.6-kb RECK transcript in a wide variety of tissues and normal cell lines, but no expression was detected in tumor cell lines. Restoration of RECK expression in tumor cell lines did not affect growth but did significantly suppress matrix invasion and metastatic activity. SDS-PAGE and gelatin zymography analysis demonstrated that due to a posttran-

scriptional event(s), secretion of MMP9 (OMIM Ref. No. 120361), a key enzyme in tumor invasion and metastasis, is decreased in cells expressing RECK. An RECK mutant lacking the C-terminal 23 residues retained the ability to suppress tumor cell invasion and MMP9 proteolytic activity but lost the ability to inhibit MMP9 release. Animal model experiments lend further support to the function of RECK. Oh et al. (2001) showed that in addition to MMP9, RECK also regulates MMP2 (OMIM Ref. No. 120360) and MT1-MMP (MMP14; 600754), which are known to be involved in cancer progression. Mice lacking a functional Reck gene died around embryonic day 10.5 with defects in collagen fibrils, the basal lamina, and vascular development; this phenotype could be partially suppressed by Mmp2 null mutation. Vascular sprouting was dramatically suppressed in tumors derived from Reck-expressing fibrosarcoma cells grown in nude mice. These results supported a role for RECK in the regulation of MMP2 in vivo and implicated RECK downregulation in tumor angiogenesis.

[8300] It is appreciated that the abovementioned animal model for RECK is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

- [8301] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8302] Takahashi, C.; Sheng, Z.; Horan, T. P.; Kitayama, H.; Maki, M.; Hitomi, K.; Kitaura, Y.; Takai, S.; Sasahara, R. M.; Hori-moto, A.; Ikawa, Y.; Ratzkin, B. J.; Arakawa, T.; Noda, M. : Regulation of matrix metalloproteinase-9 and inhibition of tumor invasion by the membrane-anchored glycoprotein RECK. Proc. Nat. Acad. Sci. 95: 13221-13226, 1998. ; and
- [8303] Oh, J.; Takahashi, R.; Kondo, S.; Mizoguchi, A.; Adachi, E.; Sasahara, R. M.; Nishimura, S.; Imamura, Y.; Kitayama, H.; Alexander, D. B.; Ide, C.; Horan, T. P.; Arakawa, T.; Yoshida, H.
- [8304] Further studies establishing the function and utilities of RECK are found in John Hopkins OMIM database record ID 605227, and in sited publications numbered 7306-7307 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tryptophan Rich Basic Protein (WRB, Accession NM_004627) is another VGAM75 host target gene. WRB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by WRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WRB BINDING SITE, designated SEQ ID:10998, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8305] Another function of VGAM75 is therefore inhibition of Tryptophan Rich Basic Protein (WRB, Accession NM_004627). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WRB. ATPase, H⁺ Transporting, Lysosomal 34kDa, V1 Subunit D (ATP6V1D, Accession NM_015994) is another VGAM75 host target gene. ATP6V1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP6V1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP6V1D BINDING SITE, designated SEQ ID:18087, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8306] Another function of VGAM75 is therefore inhibition of ATPase, H⁺ Transporting, Lysosomal 34kDa, V1 Subunit D (ATP6V1D, Accession NM_015994). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP6V1D. DNAM-1 (Accession NM_006566) is another VGAM75 host target gene. DNAM-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAM-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAM-1 BINDING SITE, designated SEQ ID:13337, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8307] Another function of VGAM75 is therefore inhibition of DNAM-1 (Accession NM_006566). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAM-1. FLJ20281 (Accession XM_165663) is another VGAM75 host target gene. FLJ20281 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20281, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20281 BINDING SITE, designated SEQ ID:43727, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8308] Another function of VGAM75 is therefore inhibition of FLJ20281 (Accession XM_165663). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20281. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM75 host target gene. GGA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GGA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE, designated SEQ ID:28919, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8309] Another function of VGAM75 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF

Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA1388 (Accession XM_168030) is another VGAM75 host target gene. KIAA1388 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1388 BINDING SITE, designated SEQ ID:44950, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8310] Another function of VGAM75 is therefore inhibition of KIAA1388 (Accession XM_168030). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1388. Protocadherin 20 (PCDH20, Accession NM_022843) is another VGAM75 host target gene. PCDH20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDH20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PCDH20 BINDING SITE, designated SEQ ID:23136, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8311] Another function of VGAM75 is therefore inhibition of Protocadherin 20 (PCDH20, Accession NM_022843). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH20. Serine/threonine Kinase 38 Like (STK38L, Accession XM_044823) is another VGAM75 host target gene. STK38L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STK38L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK38L BINDING SITE, designated SEQ ID:34294, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8312] Another function of VGAM75 is therefore inhibition of Serine/threonine Kinase 38 Like (STK38L, Accession XM_044823). Accordingly, utilities of VGAM75 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with STK38L. ZER6 (Accession XM_032742) is another VGAM75 host target gene. ZER6 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZER6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZER6 BINDING SITE, designated SEQ ID:31748, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8313] Another function of VGAM75 is therefore inhibition of ZER6 (Accession XM_032742). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZER6. LOC144893 (Accession XM_096687) is another VGAM75 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40456, to the nucleotide se-

quence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8314] Another function of VGAM75 is therefore inhibition of LOC144893 (Accession XM_096687). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC146515 (Accession XM_085493) is another VGAM75 host target gene. LOC146515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146515 BINDING SITE, designated SEQ ID:38193, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8315] Another function of VGAM75 is therefore inhibition of LOC146515 (Accession XM_085493). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146515. LOC151877 (Accession XM_098132) is another VGAM75 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41395, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8316] Another function of VGAM75 is therefore inhibition of LOC151877 (Accession XM_098132). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151877. LOC56899 (Accession NM_020140) is another VGAM75 host target gene. LOC56899 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56899 BINDING SITE, designated SEQ ID:21335, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8317] Another function of VGAM75 is therefore inhibition of LOC56899 (Accession NM_020140). Accordingly, utilities

of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56899. LOC90161 (Accession XM_029551) is another VGAM75 host target gene. LOC90161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90161 BINDING SITE, designated SEQ ID:30902, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8318] Another function of VGAM75 is therefore inhibition of LOC90161 (Accession XM_029551). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90161. LOC90538 (Accession XM_032401) is another VGAM75 host target gene. LOC90538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90538 BINDING SITE, designated SEQ ID:31655, to the nucleotide sequence of VGAM75 RNA, herein designated VGAM RNA, also designated SEQ ID:2786.

[8319] Another function of VGAM75 is therefore inhibition of LOC90538 (Accession XM_032401). Accordingly, utilities of VGAM75 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90538. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 76 (VGAM76) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8320] VGAM76 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM76 was detected is described hereinabove with reference to Figs. 1–8.

[8321] VGAM76 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murine Adenovirus A. VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8322] VGAM76 gene encodes a VGAM76 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM76 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM76 precursor RNA is designated SEQ ID:62, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:62 is located at position 2296 relative to the genome of Murine Adenovirus A.

[8323] VGAM76 precursor RNA folds onto itself, forming VGAM76 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8324] An enzyme complex designated DICER COMPLEX, `dices` the VGAM76 folded precursor RNA into VGAM76 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM76 RNA is designated SEQ ID:2787, and is provided hereinbelow with reference to the sequence listing part.

[8325] VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM76 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8326] VGAM76 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM76 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration,

Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM76 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8327] The complementary binding of VGAM76 RNA, herein designated VGAM RNA, to host target binding sites on VGAM76 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM76 host target RNA into VGAM76 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8328] It is appreciated that VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM76 host target genes. The mRNA of each one of this plurality of VGAM76 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM76 RNA, herein designated VGAM RNA, and which when bound by VGAM76 RNA causes inhibition of translation of respective one or more VGAM76 host target proteins.

[8329] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM76 gene, herein designated VGAM GENE, on one or more VGAM76 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective:

Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8330] It is yet further appreciated that a function of VGAM76 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of viral infection by Murine Adenovirus A. Specific functions, and accordingly utilities, of VGAM76 correlate with, and may be deduced from, the identity of the host target genes which VGAM76 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8331] Nucleotide sequences of the VGAM76 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM76 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM76 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM76 are further described hereinbelow with reference to Table 1.

[8332] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM76 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM76 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[8333] As mentioned hereinabove with reference to Fig. 1, a function of VGAM76 gene, herein designated VGAM is inhibition of expression of VGAM76 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM76 correlate with, and may be deduced from, the identity of the target genes which VGAM76 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8334] Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223) is a VGAM76 host target gene. ITPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR2 BINDING SITE, designated SEQ ID:7989, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8335] A function of VGAM76 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223). Accordingly, utilities of VGAM76 include di-

agnosis, prevention and treatment of diseases and clinical conditions associated with ITPR2. TNF Receptor-associated Factor 5 (TRAF5, Accession NM_004619) is another VGAM76 host target gene. TRAF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF5 BINDING SITE, designated SEQ ID:10964, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8336] Another function of VGAM76 is therefore inhibition of TNF Receptor-associated Factor 5 (TRAF5, Accession NM_004619), a gene which Member of a family of proteins that interact with TNF receptors; binds the lymphotoxin beta receptor (LTBR). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF5. The function of TRAF5 has been established by previous studies. Tumor necrosis factor (TNF; 191160) receptor-associated factors (TRAFs) are signal transducers for members of the TNF receptor superfamily (see OMIM Ref. No. 191190). TRAF

proteins are composed of an N-terminal cysteine/histidine-rich region containing zinc RING and/or zinc finger motifs, a coiled coil (leucine zipper) motif, and a homologous region in the C terminus that defines the TRAF family, the TRAF domain. The TRAF domain is involved in self-association and receptor binding. By degenerative oligonucleotide PCR amplification, Nakano et al. (1996) identified TRAF5 in the mouse and showed that it specifically interacts with the lymphotoxin-beta receptor (OMIM Ref. No. 600979) and activates the transcription factor NF-kappa-B (see OMIM Ref. No. 164011). Nakano et al. (1997) cloned the human TRAF homolog by cross hybridization with mouse TRAF5 cDNA. Their human cDNA of 2,894 bp has a 557-amino acid open reading frame that exhibits 77.5 and 80% identity to mouse TRAF5 at the nucleotide and amino acid levels, respectively. Northern blot analysis revealed that human TRAF5 mRNA is expressed in all visceral organs. Western blotting revealed that the human protein is abundantly expressed in a human follicular dendritic cell line, and to a lesser degree in several tumor cell lines. By in vitro binding, immunoprecipitation, immunoblot, and yeast 2-hybrid analyses, Aizawa et al. (1997) showed that TRAF2 (OMIM Ref. No.

601895) and TRAF5 interact with overlapping but distinct sequences in the C-terminal region of CD30 (OMIM Ref. No. 153243) and mediate the activation of NF κ B. By inter-specific backcross mapping, Nakano et al. (1997) showed that Traf5 is located in the distal region of mouse chromosome 1, which shares homology with human 1q. Fluorescence in situ hybridization confirmed the regional localization of human TRAF5 to chromosome 1q32. To investigate the functional role of Traf5 in vivo, Nakano et al. (1999) generated Traf5-deficient mice by gene targeting. They found that Traf5 $-/-$ B lymphocytes show defects in proliferation and upregulation of various surface molecules, including CD23 (OMIM Ref. No. 151445), CD54 (OMIM Ref. No. 147840), CD80 (OMIM Ref. No. 112203), CD86 (OMIM Ref. No. 601020), and FAS (OMIM Ref. No. 134637) in response to CD40 (OMIM Ref. No. 109535) stimulation. Moreover, in vitro Ig production by Traf5 $-/-$ T lymphocytes stimulated with anti-CD40 plus IL4 (OMIM Ref. No. 147780) was reduced substantially. CD27-mediated costimulatory signal also was impaired in Traf5 $-/-$ T lymphocytes. Collectively, these results demonstrated that Traf5 is involved in CD40- and CD27-mediated signaling.

- [8337] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8338] Nakano, H.; Sakon, S.; Koseki, H.; Takemori, T.; Tada, K.; Matsumoto, M.; Munechika, E.; Sakai, T.; Shirasawa, T.; Akiba, H.; Kobata, T.; Santee, S. M.; Ware, C. F.; Renner, P. D.; Taniguchi, M.; Yagita, H.; Okumura, K. : Targeted disruption of Traf5 gene causes defects in CD40- and CD27-mediated lymphocyte activation. Proc. Nat. Acad. Sci. 96: 9803-9808, 1999. ; and
- [8339] Nakano, H.; Shindo, M.; Yamada, K.; Yoshida, M. C.; Santee, S. M.; Ware, C. F.; Jenkins, N. A.; Gilbert, D. J.; Yagita, H.; Copeland, N. G.; Okumura, K. : Human TNF receptor-associated.
- [8340] Further studies establishing the function and utilities of TRAF5 are found in John Hopkins OMIM database record ID 602356, and in cited publications numbered 11509-9025 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ20296 (Accession NM_017750) is another VGAM76 host target gene. FLJ20296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20296, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20296 BINDING SITE, designated SEQ ID:19356, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8341] Another function of VGAM76 is therefore inhibition of FLJ20296 (Accession NM_017750). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20296. KIAA0574 (Accession XM_045076) is another VGAM76 host target gene. KIAA0574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0574 BINDING SITE, designated SEQ ID:34347, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8342] Another function of VGAM76 is therefore inhibition of KIAA0574 (Accession XM_045076). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0574. LOC145719 (Accession XM_096848) is another VGAM76 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40578, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8343] Another function of VGAM76 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM76 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40567, to

the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8344] Another function of VGAM76 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145720. LOC197114 (Accession XM_116987) is another VGAM76 host target gene. LOC197114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197114 BINDING SITE, designated SEQ ID:43190, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8345] Another function of VGAM76 is therefore inhibition of LOC197114 (Accession XM_116987). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197114. LOC197117 (Accession XM_116989) is another VGAM76 host target gene. LOC197117 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC197117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197117 BINDING SITE, designated SEQ ID:43197, to the nucleotide sequence of VGAM76 RNA, herein designated VGAM RNA, also designated SEQ ID:2787.

[8346] Another function of VGAM76 is therefore inhibition of LOC197117 (Accession XM_116989). Accordingly, utilities of VGAM76 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197117. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 77 (VGAM77) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8347] VGAM77 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM77 was detected is described hereinabove with reference to Figs. 1–8.

[8348] VGAM77 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Murine Adenovirus A. VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8349] VGAM77 gene encodes a VGAM77 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM77 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM77 precursor RNA is designated SEQ ID:63, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:63 is located at position 1609 relative to the genome of Murine Adenovirus A.

[8350] VGAM77 precursor RNA folds onto itself, forming VGAM77 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8351] An enzyme complex designated DICER COMPLEX, `dices` the VGAM77 folded precursor RNA into VGAM77 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM77 RNA is designated SEQ ID:2788, and is provided hereinbelow with reference to the sequence listing part.

[8352] VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM77 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8353] VGAM77 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM77 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM77 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8354] The complementary binding of VGAM77 RNA, herein designated VGAM RNA, to host target binding sites on VGAM77 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM77 host target RNA into VGAM77 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8355] It is appreciated that VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM77 host target genes. The mRNA of each one of this plurality of VGAM77 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM77 RNA, herein designated VGAM RNA, and which when bound by VGAM77 RNA causes inhibition of translation of respective one or more VGAM77 host target proteins.

[8356] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM77 gene, herein designated VGAM GENE, on one or more VGAM77 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8357] It is yet further appreciated that a function of VGAM77 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM77 include diagnosis, prevention and treatment of viral infection by Murine Adenovirus A. Specific functions, and accordingly utilities, of VGAM77 correlate with, and may be deduced from, the identity of the host target genes which VGAM77 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8358] Nucleotide sequences of the VGAM77 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM77 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM77 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM77 are further described hereinbelow with reference to Table 1.

[8359] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM77 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM77 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8360] As mentioned hereinabove with reference to Fig. 1, a function of VGAM77 gene, herein designated VGAM is inhibition of expression of VGAM77 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM77 correlate with, and may be deduced from, the identity of the target genes which VGAM77 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8361] Polymerase (DNA directed), Epsilon 3 (p17 subunit) (POLE3, Accession NM_017443) is a VGAM77 host target gene. POLE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLE3 BINDING SITE, designated SEQ ID:18900, to the nucleotide sequence of VGAM77 RNA,

herein designated VGAM RNA, also designated SEQ ID:2788.

[8362] A function of VGAM77 is therefore inhibition of Polymerase (DNA directed), Epsilon 3 (p17 subunit) (POLE3, Accession NM_017443). Accordingly, utilities of VGAM77 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLE3. Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815) is another VGAM77 host target gene. SLC5A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC5A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC5A7 BINDING SITE, designated SEQ ID:22390, to the nucleotide sequence of VGAM77 RNA, herein designated VGAM RNA, also designated SEQ ID:2788.

[8363] Another function of VGAM77 is therefore inhibition of Solute Carrier Family 5 (choline transporter), Member 7 (SLC5A7, Accession NM_021815). Accordingly, utilities of VGAM77 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC5A7.

LOC120939 (Accession XM_073688) is another VGAM77 host target gene. LOC120939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120939 BINDING SITE, designated SEQ ID:37511, to the nucleotide sequence of VGAM77 RNA, herein designated VGAM RNA, also designated SEQ ID:2788.

[8364] Another function of VGAM77 is therefore inhibition of LOC120939 (Accession XM_073688). Accordingly, utilities of VGAM77 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC120939. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 78 (VGAM78) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8365] VGAM78 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM78 was detected is described hereinabove with reference to Figs. 1–8.

[8366] VGAM78 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8367] VGAM78 gene encodes a VGAM78 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM78 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM78 precursor RNA is designated SEQ ID:64, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:64 is located at position 14370 relative to the genome of Plutella Xylostella Granulovirus.

[8368] VGAM78 precursor RNA folds onto itself, forming VGAM78 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first

half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8369] An enzyme complex designated DICER COMPLEX, `dices` the VGAM78 folded precursor RNA into VGAM78 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM78 RNA is designated SEQ ID:2789, and is provided hereinbelow with reference to the sequence listing part.

[8370] VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM78 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8371] VGAM78 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM78 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM78 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM78 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8372] The complementary binding of VGAM78 RNA, herein designated VGAM RNA, to host target binding sites on VGAM78 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM78 host target RNA into VGAM78 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8373] It is appreciated that VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM78 host target genes. The mRNA of each one of this plurality of VGAM78 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM78 RNA, herein designated VGAM RNA, and which when bound by VGAM78 RNA causes inhibition of translation of respective one or more VGAM78 host target proteins.

[8374] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM78 gene, herein designated VGAM GENE, on one or more VGAM78 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific

complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8375] It is yet further appreciated that a function of VGAM78 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM78 correlate with, and may be deduced from, the identity of the host target genes which VGAM78 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8376] Nucleotide sequences of the VGAM78 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM78 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM78 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, of VGAM78 are further described hereinbelow with reference to Table 1.

[8377] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM78 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM78 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8378] As mentioned hereinabove with reference to Fig. 1, a function of VGAM78 gene, herein designated VGAM is inhibition of expression of VGAM78 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM78 correlate with, and may be deduced from, the identity of the target genes which VGAM78 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8379] C1D (Accession NM_006333) is a VGAM78 host target gene. C1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of C1D BINDING SITE, designated SEQ ID:13032, to the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, also designated SEQ ID:2789.

[8380] A function of VGAM78 is therefore inhibition of C1D (Accession NM_006333), a gene which is similar to murine C1D and may be a component of nuclear hormone receptor complexes. Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1D. The function of C1D has been established by previous studies. Using RevErb (see OMIM Ref. No. 602408) as bait in a yeast 2-hybrid screen to identify nuclear hormone receptor corepressors, Zamir et al. (1997) cloned mouse C1d, which they called Sun-Cor, from a 17-day mouse embryo library. Sun-Cor encodes a highly basic 141-amino acid protein with a molecular mass of 16 kD. Northern blot analysis revealed expression of a 1.2-kb transcript in all 9 mouse tissues tested. Immunolocalization of Sun-Cor within transfected human kidney cells revealed a nuclear distribution. Zamir et al. (1997) determined that Sun-Cor potentiates transcriptional repression by thyroid hormone receptor and RevErb in vivo, represses transcription when fused to a heterologous DNA-binding domain, and interacts with Re-

vErb as well as with the thyroid hormone receptor in vitro. Sun-Cor also interacts with N-Cor (OMIM Ref. No. 600849) and Smrt (OMIM Ref. No. 500848) in vitro and with endogenous N-Cor in cultured cells. Zamir et al. (1997) also determined that Sun-Cor message and protein levels increase with differentiation of preadipocytes and myocytes in culture. Through mutation analysis, transfection, and expression of truncated message, they mapped the repression domain to the N-terminus. By cotransfection of RevErb and Sun-Cor followed by immunoprecipitation, direct interaction between these proteins was established. Similarly, they established direct interaction between Sun-Cor and N-Cor.

[8381] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8382] Zamir, I.; Dawson, J.; Lavinsky, R. M.; Glass, C. K.; Rosenfeld, M. G.; Lazar, M. A. : Cloning and characterization of a corepressor and potential component of the nuclear hormone receptor repression complex. Proc. Nat. Acad. Sci. 94: 14400-14405, 1997. ; and

[8383] Nehls, P.; Keck, T.; Greferath, R.; Spiess, E.; Glaser, T.; Rothbarth, K.; Stammer, H.; Werner, D. : cDNA cloning, re-

combinant expression and characterization of polypeptides with except.

[8384] Further studies establishing the function and utilities of C1D are found in John Hopkins OMIM database record ID 606997, and in cited publications numbered 5161–5164 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM_059257) is another VGAM78 host target gene. C20orf142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf142 BINDING SITE, designated SEQ ID:36932, to the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, also designated SEQ ID:2789.

[8385] Another function of VGAM78 is therefore inhibition of Chromosome 20 Open Reading Frame 142 (C20orf142, Accession XM_059257). Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf142. RI58

(Accession NM_012420) is another VGAM78 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RI58, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ ID:14797, to the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, also designated SEQ ID:2789.

[8386] Another function of VGAM78 is therefore inhibition of RI58 (Accession NM_012420). Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037) is another VGAM78 host target gene. TNRC9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNRC9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC9 BINDING SITE, designated SEQ ID:35322, to the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, also designated SEQ ID:2789.

[8387] Another function of VGAM78 is therefore inhibition of Trinucleotide Repeat Containing 9 (TNRC9, Accession XM_049037). Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC9. LOC135293 (Accession XM_072402) is another VGAM78 host target gene.

LOC135293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135293 BINDING SITE, designated SEQ ID:37494, to the nucleotide sequence of VGAM78 RNA, herein designated VGAM RNA, also designated SEQ ID:2789.

[8388] Another function of VGAM78 is therefore inhibition of LOC135293 (Accession XM_072402). Accordingly, utilities of VGAM78 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135293. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 79 (VGAM79) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8389] VGAM79 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM79 was detected is described hereinabove with reference to Figs. 1–8.

[8390] VGAM79 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8391] VGAM79 gene encodes a VGAM79 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM79 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM79 precursor RNA is designated SEQ ID:65, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:65 is located at position 44246 relative to the genome of Plutella Xylostella Granulovirus.

[8392] VGAM79 precursor RNA folds onto itself, forming VGAM79

folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8393] An enzyme complex designated DICER COMPLEX, `dices` the VGAM79 folded precursor RNA into VGAM79 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM79 RNA is designated SEQ ID:2790, and is provided hereinbelow with reference to the sequence listing part.

[8394] VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM79 host target RNA comprises three

regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8395] VGAM79 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM79 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM79 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target bind-

ing sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8396] The complementary binding of VGAM79 RNA, herein designated VGAM RNA, to host target binding sites on VGAM79 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM79 host target RNA into VGAM79 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8397] It is appreciated that VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM79 host target genes. The mRNA of each one of this plurality of VGAM79 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM79 RNA, herein designated VGAM RNA, and which when bound by VGAM79 RNA causes inhibition of translation of respective one or more VGAM79 host target proteins.

[8398] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM79 gene, herein designated VGAM GENE, on one or more VGAM79 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8399] It is yet further appreciated that a function of VGAM79 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM79 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM79 correlate with, and may be deduced from, the identity of the host target genes which VGAM79 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8400] Nucleotide sequences of the VGAM79 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM79 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM79 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM79 are further described hereinbelow with reference to Table 1.

[8401] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM79 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM79 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8402] As mentioned hereinabove with reference to Fig. 1, a function of VGAM79 gene, herein designated VGAM is inhibition of expression of VGAM79 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM79 correlate with, and may be deduced from, the identity of the target genes which VGAM79 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8403] FLJ20208 (Accession NM_017712) is a VGAM79 host tar-

get gene. FLJ20208 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20208, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20208 BINDING SITE, designated SEQ ID:19293, to the nucleotide sequence of VGAM79 RNA, herein designated VGAM RNA, also designated SEQ ID:2790.

[8404] A function of VGAM79 is therefore inhibition of FLJ20208 (Accession NM_017712). Accordingly, utilities of VGAM79 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20208. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 80 (VGAM80) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8405] VGAM80 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM80 was detected is described hereinabove with reference to Figs. 1–8.

[8406] VGAM80 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8407] VGAM80 gene encodes a VGAM80 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM80 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM80 precursor RNA is designated SEQ ID:66, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:66 is located at position 88821 relative to the genome of Plutella Xylostella Granulovirus.

[8408] VGAM80 precursor RNA folds onto itself, forming VGAM80 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide

sequence of the second half thereof.

[8409] An enzyme complex designated DICER COMPLEX, `dices` the VGAM80 folded precursor RNA into VGAM80 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM80 RNA is designated SEQ ID:2791, and is provided hereinbelow with reference to the sequence listing part.

[8410] VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM80 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8411] VGAM80 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM80 host target RNA,

herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM80 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM80 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8412] The complementary binding of VGAM80 RNA, herein designated VGAM RNA, to host target binding sites on VGAM80 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM80 host tar-

get RNA into VGAM80 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8413] It is appreciated that VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM80 host target genes. The mRNA of each one of this plurality of VGAM80 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM80 RNA, herein designated VGAM RNA, and which when bound by VGAM80 RNA causes inhibition of translation of respective one or more VGAM80 host target proteins.

[8414] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM80 gene, herein designated VGAM GENE, on one or more VGAM80 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and

Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8415] It is yet further appreciated that a function of VGAM80 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM80 correlate with, and may be deduced from, the identity of the host target genes which VGAM80 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8416] Nucleotide sequences of the VGAM80 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM80 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM80 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM80 are further described hereinbelow with reference to Table 1.

[8417] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM80 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM80 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8418] As mentioned hereinabove with reference to Fig. 1, a function of VGAM80 gene, herein designated VGAM is inhibition of expression of VGAM80 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM80 correlate with, and may be deduced from, the identity of the target genes which VGAM80 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8419] Latent Transforming Growth Factor Beta Binding Protein 1 (LTBP1, Accession NM_000627) is a VGAM80 host target gene. LTBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LTBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LTBP1 BINDING SITE, designated SEQ

ID:6242, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also designated SEQ ID:2791.

[8420] A function of VGAM80 is therefore inhibition of Latent Transforming Growth Factor Beta Binding Protein 1 (LTBP1, Accession NM_000627), a gene which is involved in assembly and secretion of latent TGF-beta. Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LTBP1. The function of LTBP1 has been established by previous studies. Transforming growth factor beta molecules (e.g., TGFB1; 190180) are synthesized and secreted as latent, inactive complexes. In platelets, the latent form of human TGFB1 includes 3 components: TGFB1, the N-terminal peptide of the TGFB1 precursor, and a novel protein called the latent TGFB1-binding protein (LTBP1 Using a cDNA clone for LTBP1, Stenman et al. (1994) assigned the gene to chromosome 2 by study of a panel of well-defined human/rodent somatic cell hybrid lines and further localized the gene to 2p12-q22 by study of 3 hybrid lines containing partially overlapping fragments of chromosome 2.

[8421] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [8422] Oklu, R.; Hesketh, R. : The latent transforming growth factor beta binding protein (LTBP) family. *Biochem. J.* 352: 601–610, 2000. ; and
- [8423] Stenman, G.; Sahlin, P.; Olofsson, A.; Geurts van Kessel, A.; Miyazono, K. : Assignment of the gene encoding the latent TGF-beta-1-binding protein (LTBP1) to human chromosome 2, region p12.
- [8424] Further studies establishing the function and utilities of LTBP1 are found in John Hopkins OMIM database record ID 150390, and in cited publications numbered 12463–12465 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prolactin Receptor (PRLR, Accession NM_000949) is another VGAM80 host target gene. PRLR BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRLR BINDING SITE, designated SEQ ID:6649, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also des-

ignated SEQ ID:2791.

[8425] Another function of VGAM80 is therefore inhibition of Prolactin Receptor (PRLR, Accession NM_000949), a gene which is a receptor for the anterior pituitary hormone prolactin. Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRLR. The function of PRLR has been established by previous studies. Owerbach et al. (1981) did Southern blot analyses of DNA from human-mouse cell hybrids to show that the prolactin gene is located on chromosome 6 (Owerbach et al., 1981). It bears homology to the genes for growth hormone (OMIM Ref. No. 139250) and chorionic somatomammotropin (OMIM Ref. No. 150200), which are on chromosome 17, but not as close homology as these two bear to each other (Cooke et al., 1981). Only 16% sequence homology of the growth hormone and prolactin gene has been found (Shome and Parlow, 1977). The regional assignment of prolactin is of interest because of possible association between prolactin-secreting adenomas and specific HLA alleles (Farid et al., 1980). Larrea et al. (1987) presented the results of family studies suggesting that there is a familial factor determining the occurrence of the 'big-big' form as the predomi-

nant immunoreactive PRL species in blood. By somatic cell hybridization, Taggart et al. (1987) narrowed the assignment of the PRL gene to 6pter–p21.1. Evans et al. (1988, 1989) mapped the prolactin gene in a series of overlapping deletions of chromosome 6 produced by gamma-irradiation of a human lymphoblastoid cell line followed by selection for HLA antigen-loss mutants. As pointed out by DiMattia (1998), the PRL gene possesses alternative tissue-specific promoters that are located 5,563 basepairs apart. The 5-prime promoter is specific for expression of prolactin in the decidualized human endometrium and in lymphoblastoid cells such as the human cell line IM-9-P3; the downstream promoter is specific for expression in the pituitary lactotrope and is under the control of the POU-homeodomain transcription factor PIT1 (OMIM Ref. No. 173110). Transcriptional control of the nonpituitary start site is linked to the differentiation of the endometrial stromal cell into the decidual cell during the secretory phase of the ovulatory cycle (DiMattia et al., 1990, Gellersen et al., 1994). By deletion analysis of the human PRL promoter in endometrial stromal cells decidualized in vitro, Watanabe et al. (2001) demonstrated a 536-bp enhancer located between nucleotides –2040 and –1505 in

the 5-prime-flanking region. DNase I footprint analysis of decidualized endometrial stromal cells revealed 3 protected regions, FP1-FP3. Transfection of overlapping 100-bp fragments of the 536-bp enhancer indicated that FP1 and FP3 each conferred enhancer activity. Gel shift assays indicated that both FP1 and FP3 bind AP1 (OMIM Ref. No. 165160), and that JUND (OMIM Ref. No. 165162) and FOSL2 (OMIM Ref. No. 601575) are components of the AP1 complex in decidual fibroblasts. Mutation of the AP1 binding site in either FP1 or FP3 decreased enhancer activity by approximately 50%, while mutation of both sites almost completely abolished activity

[8426] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8427] Watanabe, K.; Kessler, C. A.; Bachurski, C. J.; Kanda, Y.; Richardson, B. D.; Stanek, J.; Handwerger, S.; Brar, A. K. : Identification of a decidua-specific enhancer on the human prolactin gene with two critical activator protein 1 (AP-1) binding sites. *Molec. Endocr.* 15: 638-653, 2001. ; and

[8428] DiMattia, G. E.; Gellersen, B.; Duckworth, M. L.; Friesen, H. G. : Human prolactin gene expression: the use of an alter-

native noncoding exon in decidua and the IM-9-P3 lymphoblast cell.

[8429] Further studies establishing the function and utilities of PRLR are found in John Hopkins OMIM database record ID 176761, and in cited publications numbered 9717-9724 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deducator of Cyto-kinesis 3 (DOCK3, Accession XM_039259) is another VGAM80 host target gene. DOCK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOCK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOCK3 BINDING SITE, designated SEQ ID:33033, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also designated SEQ ID:2791.

[8430] Another function of VGAM80 is therefore inhibition of Deducator of Cyto-kinesis 3 (DOCK3, Accession XM_039259). Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOCK3. KIAA1483 (Accession XM_045920) is another VGAM80 host target gene.

KIAA1483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1483 BINDING SITE, designated SEQ ID:34615, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also designated SEQ ID:2791.

[8431] Another function of VGAM80 is therefore inhibition of KIAA1483 (Accession XM_045920). Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1483. SARM (Accession NM_015077) is another VGAM80 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ ID:17457, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also designated SEQ ID:2791.

[8432] Another function of VGAM80 is therefore inhibition of SARM (Accession NM_015077). Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. WD Repeat Domain 7 (WDR7, Accession NM_015285) is another VGAM80 host target gene. WDR7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WDR7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR7 BINDING SITE, designated SEQ ID:17609, to the nucleotide sequence of VGAM80 RNA, herein designated VGAM RNA, also designated SEQ ID:2791.

[8433] Another function of VGAM80 is therefore inhibition of WD Repeat Domain 7 (WDR7, Accession NM_015285). Accordingly, utilities of VGAM80 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WDR7. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 81 (VGAM81) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[8434] VGAM81 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM81 was detected is described hereinabove with reference to Figs. 1–8.

[8435] VGAM81 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8436] VGAM81 gene encodes a VGAM81 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM81 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM81 precursor RNA is designated SEQ ID:67, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:67 is located at position 95845 relative to the genome of Plutella Xylostella Granulovirus.

[8437] VGAM81 precursor RNA folds onto itself, forming VGAM81 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8438] An enzyme complex designated DICER COMPLEX, `dices` the VGAM81 folded precursor RNA into VGAM81 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM81 RNA is designated SEQ ID:2792, and is provided hereinbelow with reference to the sequence listing part.

[8439] VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM81 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8440] VGAM81 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM81 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM81 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[8441] The complementary binding of VGAM81 RNA, herein designated VGAM RNA, to host target binding sites on VGAM81 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM81 host target RNA into VGAM81 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8442] It is appreciated that VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM81 host target genes. The mRNA of each one of this plurality of VGAM81 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM81 RNA, herein designated VGAM RNA, and which when bound by VGAM81 RNA causes inhibition of translation of respective one or more VGAM81 host target proteins.

[8443] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM81 gene, herein designated VGAM GENE, on one or

more VGAM81 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8444] It is yet further appreciated that a function of VGAM81 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM81 correlate with, and may be deduced from, the identity of the host target genes which VGAM81 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8445] Nucleotide sequences of the VGAM81 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM81 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM81 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM81 are further de-
scribed hereinbelow with reference to Table 1.

[8446] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM81 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM81 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[8447] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM81 gene, herein designated VGAM is in-
hibition of expression of VGAM81 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM81 correlate with, and may be deduced from, the
identity of the target genes which VGAM81 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[8448] A Disintegrin and Metalloproteinase Domain 22 (ADAM22,
Accession NM_021722) is a VGAM81 host target gene.

ADAM22 BINDING SITE1 and ADAM22 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAM22, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM22 BINDING SITE1 and ADAM22 BINDING SITE2, designated SEQ ID:22324 and SEQ ID:22326 respectively, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8449] A function of VGAM81 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 22 (ADAM22, Accession NM_021722), a gene which Member of ADAM family of zinc metalloproteases. Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM22. The function of ADAM22 has been established by previous studies. The cellular disintegrins, also known as ADAM (a disintegrin and metalloproteinase) and MDC (metalloproteinase-like, disintegrin-like, and cysteine-rich) proteins, are potential regulators of cell-cell and cell-matrix interactions. They contain multiple regions, including pro-, metalloproteinase-like, disintegrin-like,

cysteine-rich, epidermal growth factor-like, transmembrane, and cytoplasmic domains. By radiation hybrid analysis, Poindexter et al. (1999) mapped the ADAM22 gene to chromosome 7q21.

[8450] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8451] Poindexter, K.; Nelson, N.; DuBose, R. F.; Black, R. A.; Cerretti, D. P. : The identification of seven metalloproteinase-disintegrin (ADAM) genes from genomic libraries. *Gene* 237: 61-70, 1999. ; and

[8452] Sagane, K.; Ohya, Y.; Hasegawa, Y.; Tanaka, I. : Metalloproteinase-like, disintegrin-like, cysteine-rich proteins MDC2 and MDC3: novel human cellular disintegrins highly expressed in t.

[8453] Further studies establishing the function and utilities of ADAM22 are found in John Hopkins OMIM database record ID 603709, and in cited publications numbered 528 and 11444 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0650 (Accession XM_113962) is another VGAM81 host target gene. KIAA0650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0650 BINDING SITE, designated SEQ ID:42572, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8454] Another function of VGAM81 is therefore inhibition of KIAA0650 (Accession XM_113962). Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0650. KIAA1155 (Accession XM_030864) is another VGAM81 host target gene. KIAA1155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1155 BINDING SITE, designated SEQ ID:31194, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8455] Another function of VGAM81 is therefore inhibition of KIAA1155 (Accession XM_030864). Accordingly, utilities

of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1155. NXP-2 (Accession XM_048706) is another VGAM81 host target gene. NXP-2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NXP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXP-2 BINDING SITE, designated SEQ ID:35229, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8456] Another function of VGAM81 is therefore inhibition of NXP-2 (Accession XM_048706). Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXP-2. SBBI31 (Accession NM_014035) is another VGAM81 host target gene. SBBI31 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SBBI31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBBI31 BINDING SITE, designated SEQ

ID:15265, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8457] Another function of VGAM81 is therefore inhibition of SBBI31 (Accession NM_014035). Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBBI31. LOC151248 (Accession XM_087143) is another VGAM81 host target gene. LOC151248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151248 BINDING SITE, designated SEQ ID:39085, to the nucleotide sequence of VGAM81 RNA, herein designated VGAM RNA, also designated SEQ ID:2792.

[8458] Another function of VGAM81 is therefore inhibition of LOC151248 (Accession XM_087143). Accordingly, utilities of VGAM81 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151248. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 82 (VGAM82) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8459] VGAM82 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM82 was detected is described hereinabove with reference to Figs. 1–8.

[8460] VGAM82 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8461] VGAM82 gene encodes a VGAM82 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM82 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM82 precursor RNA is designated SEQ ID:68, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:68 is located at position 37903 relative to the genome of

Plutella Xylostella Granulovirus.

[8462] VGAM82 precursor RNA folds onto itself, forming VGAM82 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8463] An enzyme complex designated DICER COMPLEX, `dices` the VGAM82 folded precursor RNA into VGAM82 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM82 RNA is designated SEQ ID:2793, and is provided hereinbelow with reference to the sequence listing part.

[8464] VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM82 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8465] VGAM82 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM82 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM82 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig.

1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8466] The complementary binding of VGAM82 RNA, herein designated VGAM RNA, to host target binding sites on VGAM82 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM82 host target RNA into VGAM82 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8467] It is appreciated that VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM82 host target genes. The mRNA of each one of this plurality of VGAM82 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM82 RNA, herein designated VGAM RNA, and which when bound by VGAM82 RNA causes inhibition of translation of respective one or more VGAM82 host target proteins.

[8468] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM82 gene, herein designated VGAM GENE, on one or more VGAM82 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8469] It is yet further appreciated that a function of VGAM82 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM82 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM82 correlate with, and may be deduced from, the identity of the host target genes which VGAM82 binds and

inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8470] Nucleotide sequences of the VGAM82 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM82 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM82 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM82 are further described hereinbelow with reference to Table 1.

[8471] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM82 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM82 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8472] As mentioned hereinabove with reference to Fig. 1, a function of VGAM82 gene, herein designated VGAM is inhibition of expression of VGAM82 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM82 correlate with, and may be deduced from, the identity of the target genes which VGAM82 binds and inhibits, and the function of these target genes, as elabo-

rated hereinbelow.

[8473] LOC145761 (Accession XM_096855) is a VGAM82 host target gene. LOC145761 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145761 BINDING SITE, designated SEQ ID:40581, to the nucleotide sequence of VGAM82 RNA, herein designated VGAM RNA, also designated SEQ ID:2793.

[8474] A function of VGAM82 is therefore inhibition of LOC145761 (Accession XM_096855). Accordingly, utilities of VGAM82 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145761. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 83 (VGAM83) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8475] VGAM83 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM83 was detected is described hereinabove with reference to Figs. 1–8.

[8476] VGAM83 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8477] VGAM83 gene encodes a VGAM83 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM83 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM83 precursor RNA is designated SEQ ID:69, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:69 is located at position 58052 relative to the genome of Plutella Xylostella Granulovirus.

[8478] VGAM83 precursor RNA folds onto itself, forming VGAM83 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is

due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8479] An enzyme complex designated DICER COMPLEX, `dices` the VGAM83 folded precursor RNA into VGAM83 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM83 RNA is designated SEQ ID:2794, and is provided hereinbelow with reference to the sequence listing part.

[8480] VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM83 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8481] VGAM83 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM83 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM83 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8482] The complementary binding of VGAM83 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM83 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM83 host target RNA into VGAM83 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8483] It is appreciated that VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM83 host target genes. The mRNA of each one of this plurality of VGAM83 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM83 RNA, herein designated VGAM RNA, and which when bound by VGAM83 RNA causes inhibition of translation of respective one or more VGAM83 host target proteins.

[8484] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM83 gene, herein designated VGAM GENE, on one or more VGAM83 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8485] It is yet further appreciated that a function of VGAM83 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM83 correlate with, and may be deduced from, the identity of the host target genes which VGAM83 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8486] Nucleotide sequences of the VGAM83 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM83 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM83 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM83 are further described hereinbelow with reference to Table 1.

[8487] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM83 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM83 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8488] As mentioned hereinabove with reference to Fig. 1, a function of VGAM83 gene, herein designated VGAM is inhibition of expression of VGAM83 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM83 correlate with, and may be deduced from, the identity of the target genes which VGAM83 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8489] Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM_006310) is a VGAM83 host target gene. NPEPPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPEPPS, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPEPPS BINDING SITE, designated SEQ ID:12995, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8490] A function of VGAM83 is therefore inhibition of Aminopeptidase Puromycin Sensitive (NPEPPS, Accession NM_006310), a gene which is puromycin-sensitive aminopeptidase and has metallopeptidase activity. Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPEPPS. The function of NPEPPS has been established by previous studies. Tobler et al. (1997) cloned PSA from a human fetal brain cDNA library using the mouse PSA cDNA as probe. They established that translation is initiated at the second of 2 possible start codons, resulting in a deduced 875-amino acid protein with a molecular mass of 99 kD by SDS-PAGE. PSA contains a zinc-binding motif conserved among gluzincin aminopeptidases and shares 98% sequence identity with the mouse protein. Northern blot analysis detected ubiquitous expression of a 4.8-kb transcript, with highest expression in brain. By in situ hybridization of adult human

brain sections, expression was localized to the perikaryon of neurons of the cortex and cerebellum. Using immunofluorescence localization of transfected HeLa cells, Tobler et al. (1997) found that PSA localizes to the perinuclear cytoplasm and shows a filamentous staining pattern. Bauer et al. (2001) cloned PSA cDNA from a human skeletal muscle library. Northern blot analysis detected major and minor transcripts of 4.8 and 4.2 kb, respectively. Huber et al. (1999) determined that PSA is identical to the metalloprotease MP100 that was originally isolated as a beta-secretase candidate from human brain by Schonlein et al. (1994). Huber et al. (1999) were able to colocalize and coimmunoprecipitate PSA with beta-amyloid precursor protein (OMIM Ref. No. 104760); however, PSA did not increase production of the amyloid-beta peptide in cotransfected cells. By RT-PCR, but not by Northern blot analysis, Bauer et al. (2001) found that PSA was upregulated in human leukemic cells following vitamin D stimulation.

[8491] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8492] Huber, G.; Thompson, A.; Gruninger, F.; Mechler, H.;

Hochstrasser, R.; Hauri, H.-P.; Malherbe, P. : cDNA cloning and molecular characterization of human brain metallo-protease MP100: a beta-secretase candidate? J. Neurochem. 72: 1215-1223, 1999. ; and

[8493] Tobler, A. R.; Constam, D. B.; Schmitt-Graff, A.; Malipiero, U.; Schlapbach, R.; Fontana, A. : Cloning of the human puromycin-sensitive aminopeptidase and evidence for expression in neu.

[8494] Further studies establishing the function and utilities of NPEPPS are found in John Hopkins OMIM database record ID 606793, and in cited publications numbered 5485-5490 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823) is another VGAM83 host target gene. PKIA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PKIA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIA BINDING SITE, designated SEQ ID:13697, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8495] Another function of VGAM83 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823). Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIA. Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630) is another VGAM83 host target gene. SLC21A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A2 BINDING SITE, designated SEQ ID:12155, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8496] Another function of VGAM83 is therefore inhibition of Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630), a gene which is a Prostaglandin transporter. Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A2. The function of SLC21A2 has been established by previ-

ous studies. At physiologic pH, prostaglandins (PGs) traverse biologic membranes poorly. Accordingly, PG transport is carrier-mediated in many tissues, including the lung, choroid plexus, liver, anterior chamber of the eye, vagina and uterus, and placenta. Kanai et al. (1995) cloned the rat prostaglandin transporter (symbolized PGT by them) and postulated 3 possible roles for the transporter. First, PGT might mediate the efflux of newly synthesized PGs from cells. Second, PGT might mediate epithelial PG transport. A third possible role of PGT is that of mediating PG clearance and degradation. Lu et al. (1996) favored the clearance role for PGT. Using a rat PGT probe on Northern blots of human kidney mRNA, they found evidence for the presence of a human PGT homolog. They screened a human kidney cDNA library and isolated human PGT. The gene encodes a 643-amino acid polypeptide with 82% identity to the rat protein. They expressed a full-length human cDNA clone in cultured cells and reported that both rat and human PGT transport PGD₂, as well as PGE₁, PGE₂, and PGF_{2a}. Although human PGT has cDNA and deduced amino acid sequences similar to those of the rat, the tissue distribution of mRNA transcripts is substantially broader in human. Additionally, the diversity

of human PGT transcripts is greater and the affinity for thromboxane-2 is greater. Lu et al. (1996) found strong PGT mRNA expression in the human fetus. By PCR-based monochromosomal somatic cell hybrid mapping and fluorescence in situ hybridization, Lu and Schuster (1998) mapped the PGT gene to 3q21.

[8497] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8498] Kanai, N.; Lu, R.; Satriano, J. A.; Bao, Y.; Wolkoff, A. W.; Schuster, V. L. : Identification and characterization of a prostaglandin transporter. Science 268: 866–869, 1995. ; and

[8499] Lu, R.; Kanai, N.; Bao, Y.; Schuster, V. L. : Cloning, in vitro expression, and tissue distribution of a human prostaglandin transporter cDNA (hPGT). J. Clin. Invest. 98: 1142–1149, 1996.

[8500] Further studies establishing the function and utilities of SLC21A2 are found in John Hopkins OMIM database record ID 601460, and in cited publications numbered 2867–2869 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp547M072 (Accession XM_028067) is another

VGAM83 host target gene. DKFZp547M072 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547M072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547M072 BINDING SITE, designated SEQ ID:30613, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8501] Another function of VGAM83 is therefore inhibition of DKFZp547M072 (Accession XM_028067). Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547M072. FLJ10761 (Accession NM_018208) is another VGAM83 host target gene. FLJ10761 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10761, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10761 BINDING SITE, designated SEQ ID:20104, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8502] Another function of VGAM83 is therefore inhibition of FLJ10761 (Accession NM_018208). Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10761. P17.3 (Accession NM_019056) is another VGAM83 host target gene. P17.3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P17.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P17.3 BINDING SITE, designated SEQ ID:21137, to the nucleotide sequence of VGAM83 RNA, herein designated VGAM RNA, also designated SEQ ID:2794.

[8503] Another function of VGAM83 is therefore inhibition of P17.3 (Accession NM_019056). Accordingly, utilities of VGAM83 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P17.3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 84 (VGAM84) viral gene, which modulates expression of respective host target genes thereof, the function and

utility of which host target genes is known in the art.

[8504] VGAM84 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM84 was detected is described hereinabove with reference to Figs. 1–8.

[8505] VGAM84 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8506] VGAM84 gene encodes a VGAM84 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM84 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM84 precursor RNA is designated SEQ ID:70, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:70 is located at position 12458 relative to the genome of Plutella Xylostella Granulovirus.

[8507] VGAM84 precursor RNA folds onto itself, forming VGAM84 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin

structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8508] An enzyme complex designated DICER COMPLEX, `dices` the VGAM84 folded precursor RNA into VGAM84 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM84 RNA is designated SEQ ID:2795, and is provided hereinbelow with reference to the sequence listing part.

[8509] VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM84 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3`

untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8510] VGAM84 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM84 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM84 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8511] The complementary binding of VGAM84 RNA, herein designated VGAM RNA, to host target binding sites on VGAM84 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM84 host target RNA into VGAM84 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8512] It is appreciated that VGAM84 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM84 host target genes. The mRNA of each one of this plurality of VGAM84 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM84 RNA, herein designated VGAM RNA, and which when bound by VGAM84 RNA causes inhibition of translation of respective one or more VGAM84 host target proteins.

[8513] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM84 gene, herein designated VGAM GENE, on one or more VGAM84 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8514] It is yet further appreciated that a function of VGAM84 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM84 correlate with, and may be deduced from, the identity of the host target genes which VGAM84 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8515] Nucleotide sequences of the VGAM84 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM84 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM84 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM84 are further described hereinbelow with reference to Table 1.

[8516] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM84 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM84 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8517] As mentioned hereinabove with reference to Fig. 1, a function of VGAM84 gene, herein designated VGAM is inhibition of expression of VGAM84 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM84 correlate with, and may be deduced from, the identity of the target genes which VGAM84 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8518] Transmembrane 4 Superfamily Member 6 (TM4SF6, Accession NM_003270) is a VGAM84 host target gene. TM4SF6 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by TM4SF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TM4SF6 BINDING SITE, designated SEQ ID:9282, to the nucleotide sequence of VGAM84 RNA, herein designated VGAM RNA, also designated SEQ ID:2795.

[8519] A function of VGAM84 is therefore inhibition of Trans-membrane 4 Superfamily Member 6 (TM4SF6, Accession NM_003270), a gene which plays a role in the regulation of cell development, activation, growth and motility. Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TM4SF6. The function of TM4SF6 has been established by previous studies. Members of the trans-membrane 4 (or tetraspanin) superfamily (TM4SF) contain 4 hydrophobic, presumably membrane-spanning sequences and a major presumed extracellular loop between the third and fourth hydrophobic domains. Several TM4SF proteins have been shown to stimulate or modulate cell growth, and some may associate with integrin and control cell adhesion and movement. Maeda et al. (1998) isolated

a human glioma cDNA that has sequence similarity to the TM4SF member TM4SF2 (OMIM Ref. No. 300096). By screening a human fetal lung cDNA library with a probe corresponding to the combined sequences of this cDNA and of an overlapping EST, they isolated cDNAs with an open reading frame encoding a deduced 245–amino acid protein termed TM4SF6. The TM4SF6 protein contains 4 putative transmembrane domains, several short cysteine motifs characteristic of TM4SF proteins, and a potential N–glycosylation site. The TM4SF6 and TM4SF2 proteins are 58% homologous. TM4SF6 was expressed as 1.9– and 1.3–kb transcripts in all human tissues examined.

[8520] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8521] Maeda, K.; Matsushashi, S.; Hori, K.; Xin, Z.; Mukai, T.; Tabuchi, K.; Egashira, M.; Niikawa, N. : Cloning and characterization of a novel human gene, TM4SF6, encoding a protein belonging to the transmembrane 4 superfamily, and mapped to Xq22. *Genomics* 52: 240–242, 1998. ; and

[8522] Todd, S. C.; Doctor, V. S.; Levy, S. : Sequences and expression of six new members of the tetraspanin/TM4SF family. *Biochim. Biophys. Acta* 1399: 101–104, 1998.

[8523] Further studies establishing the function and utilities of TM4SF6 are found in John Hopkins OMIM database record ID 300191, and in cited publications numbered 11388–11389 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1239 (Accession XM_049078) is another VGAM84 host target gene. KIAA1239 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1239, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1239 BINDING SITE, designated SEQ ID:35340, to the nucleotide sequence of VGAM84 RNA, herein designated VGAM RNA, also designated SEQ ID:2795.

[8524] Another function of VGAM84 is therefore inhibition of KIAA1239 (Accession XM_049078). Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1239. KIAA1423 (Accession XM_029703) is another VGAM84 host target gene. KIAA1423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1423, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1423 BINDING SITE, designated SEQ ID:30918, to the nucleotide sequence of VGAM84 RNA, herein designated VGAM RNA, also designated SEQ ID:2795.

[8525] Another function of VGAM84 is therefore inhibition of KIAA1423 (Accession XM_029703). Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1423. MGC23980 (Accession NM_145005) is another VGAM84 host target gene. MGC23980 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC23980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC23980 BINDING SITE, designated SEQ ID:29604, to the nucleotide sequence of VGAM84 RNA, herein designated VGAM RNA, also designated SEQ ID:2795.

[8526] Another function of VGAM84 is therefore inhibition of MGC23980 (Accession NM_145005). Accordingly, utilities of VGAM84 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC23980. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 85 (VGAM85) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8527] VGAM85 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM85 was detected is described hereinabove with reference to Figs. 1–8.

[8528] VGAM85 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8529] VGAM85 gene encodes a VGAM85 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM85 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM85 precursor RNA is designated SEQ

ID:71, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:71 is located at position 61916 relative to the genome of *Plutella Xylostella Granulovirus*.

[8530] VGAM85 precursor RNA folds onto itself, forming VGAM85 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8531] An enzyme complex designated DICER COMPLEX, `dices` the VGAM85 folded precursor RNA into VGAM85 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM85 RNA is designated SEQ ID:2796, and is provided hereinbelow with reference to the sequence list-

ing part.

[8532] VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM85 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8533] VGAM85 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM85 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM85 RNA, herein designated VGAM RNA, may have a different num-

ber of host target binding sites in untranslated regions of a VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8534] The complementary binding of VGAM85 RNA, herein designated VGAM RNA, to host target binding sites on VGAM85 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM85 host target RNA into VGAM85 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8535] It is appreciated that VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM85 host target genes. The mRNA of each one of this plurality of VGAM85 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM85 RNA, herein designated VGAM RNA, and which when bound by VGAM85 RNA causes in–

hibition of translation of respective one or more VGAM85 host target proteins.

[8536] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM85 gene, herein designated VGAM GENE, on one or more VGAM85 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8537] It is yet further appreciated that a function of VGAM85 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Gran-

ulovirus. Specific functions, and accordingly utilities, of VGAM85 correlate with, and may be deduced from, the identity of the host target genes which VGAM85 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8538] Nucleotide sequences of the VGAM85 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM85 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM85 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM85 are further described hereinbelow with reference to Table 1.

[8539] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM85 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM85 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8540] As mentioned hereinabove with reference to Fig. 1, a function of VGAM85 gene, herein designated VGAM is inhibition of expression of VGAM85 target genes. It is appreciated that specific functions, and accordingly utilities,

of VGAM85 correlate with, and may be deduced from, the identity of the target genes which VGAM85 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8541] Contactin Associated Protein-like 2 (CNTNAP2, Accession NM_014141) is a VGAM85 host target gene. CNTNAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTNAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTNAP2 BINDING SITE, designated SEQ ID:15420, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8542] A function of VGAM85 is therefore inhibition of Contactin Associated Protein-like 2 (CNTNAP2, Accession NM_014141). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTNAP2. Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943) is another VGAM85 host target gene. GRLF1 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by GRLF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRLF1 BINDING SITE, designated SEQ ID:38415, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8543] Another function of VGAM85 is therefore inhibition of Glucocorticoid Receptor DNA Binding Factor 1 (GRLF1, Accession XM_085943), a gene which inhibits transcription of the glucocorticoid receptor gene. Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRLF1. The function of GRLF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Lipin 2 (LPIN2, Accession NM_014646) is another VGAM85 host target gene. LPIN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LPIN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LPIN2 BIND-

ING SITE, designated SEQ ID:16060, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8544] Another function of VGAM85 is therefore inhibition of Lipin 2 (LPIN2, Accession NM_014646). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LPIN2. POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM_001334) is another VGAM85 host target gene. POU3F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU3F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU3F1 BINDING SITE, designated SEQ ID:29831, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8545] Another function of VGAM85 is therefore inhibition of POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM_001334), a gene which involves in early embryogenesis and neurogenesis. Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with POU3F1. The function of POU3F1 has been established by previous studies. The vertebrate class III POU transcription factors consist of 4 members: POU3F1 (Oct-6), POU3F2 (OMIM Ref. No. 600494), POU3F3 (Brain-1), and POU3F4 (Brain-4; 300039). The chromosomal locations of the murine class III POU genes were determined by interspecific backcross analysis (Avraham et al., 1993; Xia et al., 1993). On the basis of mouse-human chromosomal homologies, human POU3F1 and POU3F3 were expected to map to 1p and 2q, respectively. Sumiyama et al. (1998) found that the location of POU3F1 was consistent with this position, mapping to 1p34.1 by FISH. Contrary to the prediction, however, POU3F3 was mapped to 3p14.2 by the same method. The human POU3F2 and POU3F4 genes map to 6q16 and Xq21.1, respectively. Thus, the 4 human class III POU genes map to different chromosomes. A phylogenetic tree of these 4 genes shows that they emerged in a common ancestor of vertebrates. Studies of the genome structure of vertebrates suggest that genome duplication occurred at least twice in the early stage of vertebrate evolution; 4 homologous complexes such as Hox and MHC are interspersed in the mammalian genome. The

findings with the 4 class III POU genes are consistent with the idea of 2 genome duplications. Xia et al. (1993) mapped the mouse homolog of the POU3F1 gene, called Tst1 by them, to chromosome 4. Most mice homozygous for a mutant Pou3f1 die soon after birth (Bermingham et al., 1996; Jaegle et al., 1996).

[8546] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8547] Sumiyama, K.; Washio-Watanabe, K.; Ono, T.; Yoshida, M. C.; Hayakawa, T.; Ueda, S. : Human class III POU genes, POU3F1 and POU3F3, map to chromosomes 1p34.1 and 3p14.1. Mammalian Genome 9: 180–181, 1998. ; and

[8548] Xia, Y.-R.; Andersen, B.; Mehrabian, M.; Diep, A. T.; Warden, C. H.; Mohandas, T.; McEvilly, R. J.; Rosenfeld, M. G.; Lusk, A. J. : Chromosomal organization of mammalian POU domain factors.

[8549] Further studies establishing the function and utilities of POU3F1 are found in John Hopkins OMIM database record ID 602479, and in cited publications numbered 7963, 8632–863 and 10196 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Angiomin Like 1 (AMOTL1, Accession XM_057045)

is another VGAM85 host target gene. AMOTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMOTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOTL1 BINDING SITE, designated SEQ ID:36467, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8550] Another function of VGAM85 is therefore inhibition of Angiomotin Like 1 (AMOTL1, Accession XM_057045). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOTL1. CSRP2 Binding Protein (CSRP2BP, Accession XM_046520) is another VGAM85 host target gene. CSRP2BP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CSRP2BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSRP2BP BINDING SITE, designated SEQ ID:34736, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ

ID:2796.

[8551] Another function of VGAM85 is therefore inhibition of CSRP2 Binding Protein (CSRP2BP, Accession XM_046520). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSRP2BP. DKFZP564O0463 (Accession NM_014156) is another VGAM85 host target gene. DKFZP564O0463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0463 BINDING SITE, designated SEQ ID:15443, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8552] Another function of VGAM85 is therefore inhibition of DKFZP564O0463 (Accession NM_014156). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0463. KIAA0227 (Accession XM_027236) is another VGAM85 host target gene. KIAA0227 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by KIAA0227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0227 BINDING SITE, designated SEQ ID:30448, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8553] Another function of VGAM85 is therefore inhibition of KIAA0227 (Accession XM_027236). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0227. KIAA0618 (Accession NM_014833) is another VGAM85 host target gene. KIAA0618 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0618 BINDING SITE, designated SEQ ID:16835, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8554] Another function of VGAM85 is therefore inhibition of KIAA0618 (Accession NM_014833). Accordingly, utilities

of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0618. KIAA0711 (Accession NM_014867) is another VGAM85 host target gene. KIAA0711 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0711 BINDING SITE, designated SEQ ID:16955, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8555] Another function of VGAM85 is therefore inhibition of KIAA0711 (Accession NM_014867). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0711. KIAA1046 (Accession NM_014928) is another VGAM85 host target gene. KIAA1046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1046 BINDING SITE, designated SEQ ID:17220, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8556] Another function of VGAM85 is therefore inhibition of KIAA1046 (Accession NM_014928). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1046. Zinc Finger Protein 387 (ZNF387, Accession NM_014682) is another VGAM85 host target gene. ZNF387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF387 BINDING SITE, designated SEQ ID:16174, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8557] Another function of VGAM85 is therefore inhibition of Zinc Finger Protein 387 (ZNF387, Accession NM_014682). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF387. LOC199990 (Accession

XM_114083) is another VGAM85 host target gene.

LOC199990 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199990, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199990 BINDING SITE, designated SEQ ID:42681, to the nucleotide sequence of VGAM85 RNA, herein designated VGAM RNA, also designated SEQ ID:2796.

[8558] Another function of VGAM85 is therefore inhibition of LOC199990 (Accession XM_114083). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199990. LOC91170 (Accession XM_036612) is another VGAM85 host target gene. LOC91170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91170 BINDING SITE, designated SEQ ID:32480, to the nucleotide sequence of VGAM85 RNA, herein designated

VGAM RNA, also designated SEQ ID:2796.

[8559] Another function of VGAM85 is therefore inhibition of LOC91170 (Accession XM_036612). Accordingly, utilities of VGAM85 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91170. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 86 (VGAM86) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8560] VGAM86 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM86 was detected is described hereinabove with reference to Figs. 1–8.

[8561] VGAM86 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8562] VGAM86 gene encodes a VGAM86 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM86 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM86 precursor RNA is designated SEQ ID:72, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:72 is located at position 28852 relative to the genome of *Plutella Xylostella Granulovirus*.

[8563] VGAM86 precursor RNA folds onto itself, forming VGAM86 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8564] An enzyme complex designated DICER COMPLEX, `dices` the VGAM86 folded precursor RNA into VGAM86 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM86 RNA is designated SEQ ID:2797, and is provided hereinbelow with reference to the sequence listing part.

[8565] VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM86 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[8566] VGAM86 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM86 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM86 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8567] The complementary binding of VGAM86 RNA, herein designated VGAM RNA, to host target binding sites on VGAM86 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM86 host target RNA into VGAM86 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8568] It is appreciated that VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM86 host target genes. The mRNA of each one of this plurality of VGAM86 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM86 RNA, herein designated VGAM RNA, and which when bound by VGAM86 RNA causes inhibition of translation of respective one or more VGAM86 host target proteins.

[8569] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM86 gene, herein designated VGAM GENE, on one or more VGAM86 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8570] It is yet further appreciated that a function of VGAM86 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM86 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM86 correlate with, and may be deduced from, the identity of the host target genes which VGAM86 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8571] Nucleotide sequences of the VGAM86 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM86 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM86 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM86 are further described hereinbelow with reference to Table 1.

[8572] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM86 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM86 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8573] As mentioned hereinabove with reference to Fig. 1, a function of VGAM86 gene, herein designated VGAM is inhibition of expression of VGAM86 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM86 correlate with, and may be deduced from, the identity of the target genes which VGAM86 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8574] HCGIV.9 (Accession NM_018985) is a VGAM86 host target gene. HCGIV.9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HCGIV.9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCGIV.9 BINDING SITE, designated SEQ ID:21056, to the nucleotide sequence of VGAM86 RNA, herein designated VGAM RNA, also designated SEQ ID:2797.

[8575] A function of VGAM86 is therefore inhibition of HCGIV.9 (Accession NM_018985). Accordingly, utilities of VGAM86 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCGIV.9. LOC127534 (Accession XM_060532) is another VGAM86

host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37162, to the nucleotide sequence of VGAM86 RNA, herein designated VGAM RNA, also designated SEQ ID:2797.

[8576] Another function of VGAM86 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM86 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC222171 (Accession XM_166586) is another VGAM86 host target gene. LOC222171 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222171, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222171 BINDING SITE, designated SEQ ID:44557, to the nucleotide sequence of VGAM86 RNA, herein designated VGAM RNA, also designated SEQ ID:2797.

[8577] Another function of VGAM86 is therefore inhibition of LOC222171 (Accession XM_166586). Accordingly, utilities of VGAM86 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222171. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 87 (VGAM87) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8578] VGAM87 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM87 was detected is described hereinabove with reference to Figs. 1–8.

[8579] VGAM87 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8580] VGAM87 gene encodes a VGAM87 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM87

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM87 precursor RNA is designated SEQ ID:73, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:73 is located at position 79962 relative to the genome of *Plutella Xylostella Granulovirus*.

[8581] VGAM87 precursor RNA folds onto itself, forming VGAM87 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8582] An enzyme complex designated DICER COMPLEX, `dices` the VGAM87 folded precursor RNA into VGAM87 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 78%) nucleotide sequence of VGAM87 RNA is designated SEQ ID:2798, and is provided hereinbelow with reference to the sequence listing part.

[8583] VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM87 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8584] VGAM87 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM87 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host tar-

get binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM87 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8585] The complementary binding of VGAM87 RNA, herein designated VGAM RNA, to host target binding sites on VGAM87 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM87 host target RNA into VGAM87 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8586] It is appreciated that VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM87 host target genes. The mRNA of each one of this plurality of VGAM87 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM87 RNA, herein designated VGAM RNA, and which when bound by VGAM87 RNA causes inhibition of translation of respective one or more VGAM87 host target proteins.

[8587] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM87 gene, herein designated VGAM GENE, on one or more VGAM87 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8588] It is yet further appreciated that a function of VGAM87 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM87 correlate with, and may be deduced from, the identity of the host target genes which VGAM87 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8589] Nucleotide sequences of the VGAM87 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM87 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM87 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM87 are further described hereinbelow with reference to Table 1.

[8590] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM87 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM87 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8591] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM87 gene, herein designated VGAM is inhibition of expression of VGAM87 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM87 correlate with, and may be deduced from, the identity of the target genes which VGAM87 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8592] Plexin B2 (PLXNB2, Accession NM_012401) is a VGAM87 host target gene. PLXNB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLXNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLXNB2 BINDING SITE, designated SEQ ID:14778, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8593] A function of VGAM87 is therefore inhibition of Plexin B2 (PLXNB2, Accession NM_012401), a gene which is a novel member of the plexin family. Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLXNB2. The function of PLXNB2 has been established by previous

studies. Using the technique of differential display, Shinoura et al. (1995) identified a cDNA fragment that was differentially expressed in malignant vs benign brain tumors. By screening a human fetal brain cDNA library with this fragment, they isolated a novel cDNA, which they termed MM1. MM1 was expressed almost 8-fold higher in glioblastomas compared to low-grade astrocytomas and slightly higher in malignant meningiomas than in benign meningiomas. By screening human brain cDNAs for those encoding proteins larger than 60 kD, Nagase et al. (1997) identified the MM1 gene, which they called KIAA0315. By RT-PCR amplification starting from the partial cDNA sequences of clones MM1 and KIAA0315, Tamagnone et al. (1999) identified the cDNA sequence of a novel member of the plexin gene family and named the gene plexin B2. Using a radiation hybrid mapping panel, Nagase et al. (1997) mapped the PLXNB2 gene to chromosome 22. By sequence analysis, Tamagnone et al. (1999) showed that the PLXNB2 gene maps to 22q13.31-q13.33 in the BAC clone (GenBank AL022328) containing the MAPK12 (OMIM Ref. No. 602399) and MAPK11 (OMIM Ref. No. 602898) genes.

[8594] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [8595] Shinoura, N.; Shamraj, O. I.; Hugenholtz, H.; Zhu, J. G.; McBlack, P.; Warnick, R.; Tew, J. J.; Wani, M. A.; Menon, A. G. : Identification and partial sequence of a cDNA that is differentially expressed in human brain tumors. *Cancer Lett.* 89: 215–221, 1995. ; and
- [8596] Tamagnone, L.; Artigiani, S.; Chen, H.; He, Z.; Ming, G.; Song, H.; Chedotal, A.; Winberg, M. L.; Goodman, C. S.; Poo, M.; Tessier-Lavigne, M.; Comoglio, P. M. : Plexins are a large fam.
- [8597] Further studies establishing the function and utilities of PLXNB2 are found in John Hopkins OMIM database record ID 604293, and in cited publications numbered 957, 707 and 7272 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983) is another VGAM87 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10128, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8598] Another function of VGAM87 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter, γ^+ system), Member 6 (SLC7A6, Accession NM_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 has been established by previous studies. Using RT-PCR with degenerate primers to screen for amino acid transporters in opossum kidney, followed by searching EST databases, Torrents et al. (1998) obtained a cDNA encoding SLC7A6, which they called $\gamma(+)$ LAT2. SLC7A6 is identical to the KIAA0245 gene reported by Nagase et al. (1996). Sequence analysis predicted that SLC7A6 is a 515-amino acid, typical organic solute transporter protein with 12 transmembrane domains, 3 potential phosphorylation sites, and N- and C-terminal cytoplasmic segments. SLC7A6 shares 75% amino acid identity with the opossum sequence and $\gamma(+)$ LAT1 (SLC7A7; 603593). By RT-PCR

analysis, Nagase et al. (1996) detected SLC7A6 expression in all tissues tested except liver; expression was weak in pancreas and highest in thymus.

[8599] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8600] Nagase, T.; Seki, N.; Ishikawa, K.; Ohira, M.; Kawarabayasi, Y.; Ohara, O.; Tanaka, A.; Kotani, H.; Miyajima, N.; Nomura, N. : Prediction of the coding sequences of unidentified human genes. VI. The coding sequences of 80 new genes (KIAA0201–KIAA0280) deduced by analysis of cDNA clones from cell line KG–1 and brain. DNA Res. 3: 321–329, 1996. ; and

[8601] Torrents, D.; Estevez, R.; Pineda, M.; Fernandez, E.; Lloberas, J.; Shi, Y.–B.; Zorzano, A.; Palacin, M. : Identification and characterization of a membrane protein (y(+))L amino acid tr.

[8602] Further studies establishing the function and utilities of SLC7A6 are found in John Hopkins OMIM database record ID 605641, and in cited publications numbered 9379 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitin Fusion Degradation 1–like (UFD1L, Accession XM_055490) is an–

other VGAM87 host target gene. UFD1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UFD1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UFD1L BINDING SITE, designated SEQ ID:36275, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8603] Another function of VGAM87 is therefore inhibition of Ubiquitin Fusion Degradation 1-like (UFD1L, Accession XM_055490), a gene which is essential component of the ubiquitin-dependent proteolytic pathway . Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UFD1L. The function of UFD1L has been established by previous studies. In a search for genes in the 22q11.2 region possibly implicated in the DiGeorge syndrome (OMIM Ref. No. 188400), Pizutti et al. (1997) identified a gene whose functional features and tissue-specific expression suggested a distinct role in embryogenesis. Symbolized UFD1L by them (for ubiquitin fusion degradation 1-like), the gene encodes the human homolog of the

yeast ubiquitin fusion degradation 1 (UFD1) protein that is involved in the degradation of ubiquitin fusion proteins (see OMIM Ref. No. 191320). Cloning and characterization of the murine homolog (Ufd1l) showed it to be expressed during embryogenesis in the eyes and in the inner ear primordia. These findings suggested to Pizutti et al. (1997) that the proteolytic pathway recognizing ubiquitin fusion proteins for degradation is conserved in vertebrates and that UFD1L gene hemizyosity may be the cause of some of the CATCH22-associated developmental defects. The basic helix-loop-helix transcription factor dHAND (HAND2; 602407) is required for survival of cells in the neural crest-derived branchial and aortic arch arteries and the right ventricle. Mice lacking endothelin-1 (EDN1; 131240) have cardiac and cranial neural crest defects typical of the 22q11 deletion syndrome and display down-regulation of dHAND, suggesting that a molecular pathway involving dHAND may be disrupted in that syndrome. The HAND2, EDN1, and ET1 receptor (EDNRA; 131243) genes do not map to 22q11, the DiGeorge syndrome critical region, in humans. In a screen for mouse genes dependent on dHAND, Yamagishi et al. (1999) identified Ufd1, which maps to human 22q11 and encodes a protein

involved in degradation of ubiquitinated proteins. Mouse Ufd1 was specifically expressed in most tissues affected in patients with the DiGeorge (22q11 deletion) syndrome. Yamagishi et al. (1999) found, furthermore, that the human UFD1L gene was deleted in all 182 patients studied with the 22q11 deletion, and a smaller deletion of approximately 20 kb that removed exons 1 to 3 of UFD1L was found in 1 individual with features typical of 22q11 deletion syndrome. In the individual with the smaller deletion, patient J.F., Yamagishi et al. (1999) found that the CDC45L gene (OMIM Ref. No. 603465), which is immediately telomeric of UFD1L, was the site of the deletion in the region between exons 5 and 6 of the 5-prime breakpoint. They considered that the deletion in CDC45L may act as a modifier of the phenotype in patient J.F. UFD1L and CDC45L are transcribed in opposite directions. The deletion left exons 4 to 12 of UFD1L intact; the first 5 exons of CDC45L were deleted. Patient J.F. had nearly all of the features commonly associated with the 2-Mb 22q11 deletion. Four days after birth the patient was diagnosed with interrupted aortic arch, persistent truncus arteriosus, cleft palate, small mouth, low-set ears, broad nasal bridge, neonatal hypocalcemia, T-lymphocyte deficiency,

and syndactyly of her toes. The deletion was not present in her parents or in 100 control subjects.

[8604] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8605] Pizutti, A.; Novelli, G.; Ratti, A.; Amati, F.; Mari, A.; Calabrese, G.; Nicolis, S.; Silani, V.; Marino, B.; Scarlato, G.; Ottolenghi, S.; Dallapiccola, B. : UFD1L, a developmentally expressed ubiquitination gene, is deleted in CATCH 22 syndrome. Hum. Molec. Genet. 6: 259–265, 1997. ; and

[8606] Yamagishi, H.; Garg, V.; Matsuoka, R.; Thomas, T.; Srivastava, D. : A molecular pathway revealing a genetic basis for human cardiac and craniofacial defects. Science 283: 1158–1161, 199.

[8607] Further studies establishing the function and utilities of UFD1L are found in John Hopkins OMIM database record ID 601754, and in cited publications numbered 6233–6234 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BANP (Accession XM_038696) is another VGAM87 host target gene. BANP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BANP, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BANP BINDING SITE, designated SEQ ID:32911, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8608] Another function of VGAM87 is therefore inhibition of BANP (Accession XM_038696). Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BANP. Chromosome 20 Open Reading Frame 59 (C20orf59, Accession NM_022082) is another VGAM87 host target gene. C20orf59 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf59 BINDING SITE, designated SEQ ID:22624, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8609] Another function of VGAM87 is therefore inhibition of Chromosome 20 Open Reading Frame 59 (C20orf59, Accession NM_022082). Accordingly, utilities of VGAM87 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf59. CLIPR-59 (Accession NM_015526) is another VGAM87 host target gene. CLIPR-59 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CLIPR-59, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLIPR-59 BINDING SITE, designated SEQ ID:17786, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8610] Another function of VGAM87 is therefore inhibition of CLIPR-59 (Accession NM_015526). Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLIPR-59. FLJ10898 (Accession XM_002486) is another VGAM87 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE,

designated SEQ ID:29890, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8611] Another function of VGAM87 is therefore inhibition of FLJ10898 (Accession XM_002486). Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. KIAA0350 (Accession XM_028332) is another VGAM87 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30664, to the nucleotide sequence of VGAM87 RNA, herein designated VGAM RNA, also designated SEQ ID:2798.

[8612] Another function of VGAM87 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities of VGAM87 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 88 (VGAM88) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8613] VGAM88 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM88 was detected is described hereinabove with reference to Figs. 1–8.

[8614] VGAM88 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8615] VGAM88 gene encodes a VGAM88 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM88 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM88 precursor RNA is designated SEQ ID:74, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:74 is located at position 66710 relative to the genome of

Plutella Xylostella Granulovirus.

[8616] VGAM88 precursor RNA folds onto itself, forming VGAM88 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8617] An enzyme complex designated DICER COMPLEX, `dices` the VGAM88 folded precursor RNA into VGAM88 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM88 RNA is designated SEQ ID:2799, and is provided hereinbelow with reference to the sequence listing part.

[8618] VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA,

VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM88 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8619] VGAM88 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM88 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM88 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig.

1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8620] The complementary binding of VGAM88 RNA, herein designated VGAM RNA, to host target binding sites on VGAM88 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM88 host target RNA into VGAM88 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8621] It is appreciated that VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM88 host target genes. The mRNA of each one of this plurality of VGAM88 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM88 RNA, herein designated VGAM RNA, and which when bound by VGAM88 RNA causes inhibition of translation of respective one or more VGAM88 host target proteins.

[8622] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM88 gene, herein designated VGAM GENE, on one or more VGAM88 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8623] It is yet further appreciated that a function of VGAM88 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM88 correlate with, and may be deduced from, the identity of the host target genes which VGAM88 binds and

inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8624] Nucleotide sequences of the VGAM88 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM88 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM88 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM88 are further described hereinbelow with reference to Table 1.

[8625] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM88 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM88 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8626] As mentioned hereinabove with reference to Fig. 1, a function of VGAM88 gene, herein designated VGAM is inhibition of expression of VGAM88 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM88 correlate with, and may be deduced from, the identity of the target genes which VGAM88 binds and inhibits, and the function of these target genes, as elabo-

rated hereinbelow.

[8627] Actinin, Alpha 2 (ACTN2, Accession NM_001103) is a VGAM88 host target gene. ACTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTN2 BINDING SITE, designated SEQ ID:6759, to the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, also designated SEQ ID:2799.

[8628] A function of VGAM88 is therefore inhibition of Actinin, Alpha 2 (ACTN2, Accession NM_001103), a gene which an actin-binding protein with multiple roles in different cell types. Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTN2. The function of ACTN2 has been established by previous studies. Alpha-actinin is an actin-binding protein with multiple roles in different cell types. In nonmuscle cells, the cytoskeletal isoform is found along microfilament bundles and adherens-type junctions, where it is involved in binding actin to the membrane (see OMIM Ref. No. ACTN1; 102575). In con-

trast, skeletal, cardiac, and smooth muscle isoforms are localized to the Z-disc and analogous dense bodies, where they help anchor the myofibrillar actin filaments. Beggs et al. (1992) characterized 2 human muscle-specific alpha-actinin genes, ACTN2 and ACTN3 (OMIM Ref. No. 102574). Using somatic cell hybrids, Beggs et al. (1992) mapped the ACTN2 and ACTN3 genes to chromosomes 1 and 11, respectively. In situ hybridization placed the ACTN2 locus at 1q42-q43. Beggs et al. (1992) identified a polymorphic (CA)_n repeat within the ACTN2 gene and used it to position the ACTN2 gene on the CEPH linkage map of chromosome 1.

[8629] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8630] Beggs, A. H.; Byers, T. J.; Knoll, J. H. M.; Boyce, F. M.; Bruns, G. A. P.; Kunkel, L. M. : Cloning and characterization of two human skeletal muscle alpha-actinin genes located on chromosomes 1 and 11. J. Biol. Chem. 267: 9281-9288, 1992. ; and

[8631] Beggs, A. H.; Phillips, H. A.; Kozman, H.; Mulley, J. C.; Wilton, S. D.; Kunkel, L. M.; Laing, N. G. : A (CA)_n repeat polymorphism for the human skeletal muscle alpha-ac-

tinin gene ACTN2.

[8632] Further studies establishing the function and utilities of ACTN2 are found in John Hopkins OMIM database record ID 102573, and in cited publications numbered 4264–4266 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191) is another VGAM88 host target gene. C1orf22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf22 BINDING SITE, designated SEQ ID:24840, to the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, also designated SEQ ID:2799.

[8633] Another function of VGAM88 is therefore inhibition of Chromosome 1 Open Reading Frame 22 (C1orf22, Accession NM_025191). Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf22. LOC114932 (Accession XM_052614) is another VGAM88 host target

gene. LOC114932 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC114932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114932 BINDING SITE, designated SEQ ID:36004, to the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, also designated SEQ ID:2799.

[8634] Another function of VGAM88 is therefore inhibition of LOC114932 (Accession XM_052614). Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114932. LOC119369 (Accession XM_061434) is another VGAM88 host target gene. LOC119369 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC119369, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119369 BINDING SITE, designated SEQ ID:37206, to the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, also designated SEQ ID:2799.

[8635] Another function of VGAM88 is therefore inhibition of LOC119369 (Accession XM_061434). Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119369. LOC255533 (Accession XM_173073) is another VGAM88 host target gene. LOC255533 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255533, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255533 BINDING SITE, designated SEQ ID:46330, to the nucleotide sequence of VGAM88 RNA, herein designated VGAM RNA, also designated SEQ ID:2799.

[8636] Another function of VGAM88 is therefore inhibition of LOC255533 (Accession XM_173073). Accordingly, utilities of VGAM88 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255533. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 89 (VGAM89) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[8637] VGAM89 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM89 was detected is described hereinabove with reference to Figs. 1–8.

[8638] VGAM89 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8639] VGAM89 gene encodes a VGAM89 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM89 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM89 precursor RNA is designated SEQ ID:75, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:75 is located at position 9283 relative to the genome of Plutella Xylostella Granulovirus.

[8640] VGAM89 precursor RNA folds onto itself, forming VGAM89 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8641] An enzyme complex designated DICER COMPLEX, `dices` the VGAM89 folded precursor RNA into VGAM89 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM89 RNA is designated SEQ ID:2800, and is provided hereinbelow with reference to the sequence listing part.

[8642] VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM89 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8643] VGAM89 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM89 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM89 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[8644] The complementary binding of VGAM89 RNA, herein designated VGAM RNA, to host target binding sites on VGAM89 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM89 host target RNA into VGAM89 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8645] It is appreciated that VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM89 host target genes. The mRNA of each one of this plurality of VGAM89 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM89 RNA, herein designated VGAM RNA, and which when bound by VGAM89 RNA causes inhibition of translation of respective one or more VGAM89 host target proteins.

[8646] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM89 gene, herein designated VGAM GENE, on one or

more VGAM89 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8647] It is yet further appreciated that a function of VGAM89 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM89 correlate with, and may be deduced from, the identity of the host target genes which VGAM89 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8648] Nucleotide sequences of the VGAM89 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM89 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM89 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM89 are further de-
scribed hereinbelow with reference to Table 1.

[8649] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM89 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM89 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[8650] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM89 gene, herein designated VGAM is in-
hibition of expression of VGAM89 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM89 correlate with, and may be deduced from, the
identity of the target genes which VGAM89 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[8651] Inhibin, Beta C (INHBC, Accession NM_005538) is a
VGAM89 host target gene. INHBC BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by INHBC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INHBC BINDING SITE, designated SEQ ID:12064, to the nucleotide sequence of VGAM89 RNA, herein designated VGAM RNA, also designated SEQ ID:2800.

[8652] A function of VGAM89 is therefore inhibition of Inhibin, Beta C (INHBC, Accession NM_005538), a gene which inhibits the secretion of follitropin by the pituitary gland. Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INHBC. The function of INHBC has been established by previous studies. Activins are homo- or heterodimers of related beta subunits (see OMIM Ref. No. 147290) while inhibins are dimers composed of an alpha subunit (OMIM Ref. No. 147380) and an activin beta subunit (summarized in Schmitt et al., 1996). These proteins belong to the TGF-beta superfamily (see OMIM Ref. No. 190180), the members of which have important roles in cell determination, differentiation, and growth. Members of the inhibin/activin subgroup were originally identified

by their opposing roles in the control of follicle-stimulating hormone (OMIM Ref. No. 118850) release by cultured pituitary cells (Ling et al., 1986). Activin ligands act as growth and differentiation factors in many cells and tissues. Mellor et al. (2000) examined the localization of and dimerization among activin subunits. The results demonstrated that activin beta-C can form dimers with activin beta-A and beta-B in vitro, but not with the inhibin alpha subunit. Using a specific antibody, activin beta-C protein was localized to human liver and prostate and colocalized with beta-A and beta-B subunits to specific cell types in benign and malignant prostate tissues. The capacity to form novel activin heterodimers (but not inhibin C) appears to reside in the human liver and prostate. The authors concluded that formation of activin AC or BC heterodimers may have significant implications in the regulation of levels and/or biologic activity of other activins in these tissues.

[8653] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8654] Schmitt, J.; Hotten, G.; Jenkins, N. A.; Gilbert, D. J.; Copeland, N. G.; Pohl, J.; Schrewe, H. : Structure, chromo-

somal localization, and expression analysis of the mouse inhibin/activin betaC (Inhbc) gene. Genomics 32: 358–366, 1996. ; and

[8655] Mellor, S. L.; Cranfield, M.; Ries, R.; Pedersen, J.; Cancilla, B.; de Kretser, D.; Groome, N. P.; Mason, A. J.; Risbridger, G. P. : Localization of activin beta(A)–, beta(B)–, and beta(C)–.

[8656] Further studies establishing the function and utilities of INHBC are found in John Hopkins OMIM database record ID 601233, and in cited publications numbered 2834–283 and 5243 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pleiomorphic Adenoma Gene–like 1 (PLAGL1, Accession NM_002656) is another VGAM89 host target gene. PLAGL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAGL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAGL1 BINDING SITE, designated SEQ ID:8530, to the nucleotide sequence of VGAM89 RNA, herein designated VGAM RNA, also designated SEQ ID:2800.

[8657] Another function of VGAM89 is therefore inhibition of

Pleiomorphic Adenoma Gene-like 1 (PLAGL1, Accession NM_002656), a gene which regulates apoptosis and cell cycle arrest. Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAGL1. The function of PLAGL1 has been established by previous studies. Cell proliferation is regulated through connected molecular pathways controlling cell division, differentiation, growth arrest, and apoptosis. A tight control of these events is necessary to the maintenance of homeostasis from development to senescence and involves multiple genes. Dysregulation of some of these genes can lead to pathologic situations such as neurodegenerative disorders, immunodeficiency syndromes, and cancer. Early studies on tumor development focused on oncogenes, the genes whose gain of function leads to enhanced cell growth. The inactivation of a tumor suppressor gene, in contrast, can contribute to the growth deregulation of a tumor cell. This tumor suppressor gene inactivation can occur through a loss-of-function mutation accompanied by a loss of heterozygosity, homozygous deletion, or epigenetic mechanisms. Several lines of evidence suggest a tumor suppressor function to a candidate gene: involvement in familial

predisposition to cancer, inactivation in human tumors, tumor formation in null-mutant mice, and functional properties compatible with a role in cell proliferation or development. The candidates in which all of these criteria had been fulfilled include p53 (OMIM Ref. No. 191170), RB (OMIM Ref. No. 180200), p16 (OMIM Ref. No. 600160), and VHL (OMIM Ref. No. 193300). Spengler et al. (1997) isolated a novel mouse gene, designated Zac, which encodes a protein with 7 zinc fingers of the C2H2 type that is only distantly related to previously isolated zinc finger proteins and that inhibits tumor cell proliferation in vitro and in vivo in nude mice. They showed that these antiproliferative properties ensued from the regulation of 2 pathways critical to the activity of p53, i.e., cell cycle progression and apoptosis. Thus, mouse Zac was the first gene unrelated to p53 that was found to regulate these 2 fundamental genetic programs. The authors hypothesized that Zac also could share with p53 its tumor suppressor activity and isolated the human homolog of Zac to investigate its putative tumor suppressor function. They found that human ZAC is a widely expressed zinc finger protein that shows transactivation and DNA-binding activities. Furthermore, like its mouse counterpart and p53, ZAC in-

hibits tumor cell proliferation through the induction of both apoptosis and cell cycle arrest. Kamiya et al. (2000) described a screen for new imprinted human genes, and in this way identified the ZAC/PLAGL1 gene as a strong candidate for transient neonatal diabetes mellitus (TNDM; 601410). To screen for imprinted genes, they compared parthenogenetic DNA from a chimeric patient FD and androgenetic DNA from hydatidiform mole, using restriction landmark genome scanning for methylation. This resulted in identification of 2 novel imprinted loci, one of which (NV149) mapped to the TNDM region of 6q24. From analysis of the corresponding genomic region, it was determined that NV149 lies approximately 60 kb upstream of the ZAC/PLAGL1 gene. RT-PCR analysis was used to confirm that the ZAC/PLAGL1 gene is expressed only from the paternal allele in a variety of tissues. TNDM is known to result from upregulation of a paternally expressed gene on 6q24. Kamiya et al. (2000) pointed to the paternal expression, map position, and known biologic properties of ZAC/PLAGL1 as making it highly likely that it is the TNDM gene. In particular, ZAC/PLAGL1 is a transcriptional regulator of the type 1 receptor for pituitary adenylate cyclase-activating polypeptide (OMIM Ref. No. 102981), which is

the most potent known insulin secretagogue and an important mediator of autocrine control of insulin secretion in the pancreatic islet.

[8658] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8659] Spengler, D.; Villalba, M.; Hoffmann, A.; Pantaloni, C.; Houssami, S.; Bockaert, J.; Journot, L. : Regulation of apoptosis and cell cycle arrest by Zac1, a novel zinc finger protein expressed in the pituitary gland and the brain. EMBO J. 16: 2814–2825, 1997. ; and

[8660] Kamiya, M.; Judson, H.; Okazaki, Y.; Kusakabe, M.; Muramatsu, M.; Takada, S.; Takagi, N.; Arima, T.; Wake, N.; Kamimura, K.; Satomura, K.; Hermann, R.; Bonthron, D. T.; Hayashizaki, Y. :.

[8661] Further studies establishing the function and utilities of PLAGL1 are found in John Hopkins OMIM database record ID 603044, and in cited publications numbered 8651–8652, 7188, 8653–8647, 684 and 8648–8649 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434G1411 (Accession XM_166383) is another VGAM89 host target gene. DKFZP434G1411 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by DKFZP434G1411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434G1411 BINDING SITE, designated SEQ ID:44232, to the nucleotide sequence of VGAM89 RNA, herein designated VGAM RNA, also designated SEQ ID:2800.

[8662] Another function of VGAM89 is therefore inhibition of DKFZP434G1411 (Accession XM_166383). Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434G1411. LOC91409 (Accession XM_038298) is another VGAM89 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32804, to the nucleotide sequence of VGAM89 RNA, herein designated VGAM RNA, also designated SEQ ID:2800.

[8663] Another function of VGAM89 is therefore inhibition of

LOC91409 (Accession XM_038298). Accordingly, utilities of VGAM89 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 90 (VGAM90) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8664] VGAM90 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM90 was detected is described hereinabove with reference to Figs. 1–8.

[8665] VGAM90 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8666] VGAM90 gene encodes a VGAM90 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM90 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM90 precursor RNA is designated SEQ ID:76, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:76 is located at position 15285 relative to the genome of *Plutella Xylostella Granulovirus*.

[8667] VGAM90 precursor RNA folds onto itself, forming VGAM90 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8668] An enzyme complex designated DICER COMPLEX, `dices` the VGAM90 folded precursor RNA into VGAM90 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM90 RNA is designated SEQ ID:2801, and is provided hereinbelow with reference to the sequence listing part.

[8669] VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM90 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[8670] VGAM90 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM90 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustra-

tion only, and is not meant to be limiting – VGAM90 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8671] The complementary binding of VGAM90 RNA, herein designated VGAM RNA, to host target binding sites on VGAM90 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM90 host target RNA into VGAM90 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8672] It is appreciated that VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM90 host target genes. The mRNA of each one of this plurality of VGAM90 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM90 RNA, herein designated VGAM RNA, and which when bound by VGAM90 RNA causes inhibition of translation of respective one or more VGAM90 host target proteins.

- [8673] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM90 gene, herein designated VGAM GENE, on one or more VGAM90 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [8674] It is yet further appreciated that a function of VGAM90 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM90 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM90 correlate with, and may be deduced from, the identity of the host target genes which VGAM90 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8675] Nucleotide sequences of the VGAM90 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM90 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM90 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM90 are further described hereinbelow with reference to Table 1.

[8676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM90 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM90 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8677] As mentioned hereinabove with reference to Fig. 1, a function of VGAM90 gene, herein designated VGAM is in-

hibition of expression of VGAM90 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM90 correlate with, and may be deduced from, the identity of the target genes which VGAM90 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8678] Aldehyde Dehydrogenase 3 Family, Member A2 (ALDH3A2, Accession XM_045060) is a VGAM90 host target gene. ALDH3A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH3A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH3A2 BINDING SITE, designated SEQ ID:34337, to the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8679] A function of VGAM90 is therefore inhibition of Aldehyde Dehydrogenase 3 Family, Member A2 (ALDH3A2, Accession XM_045060). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH3A2. Bone Morphogenetic Protein Receptor, Type IA (BMPR1A, Accession

NM_004329) is another VGAM90 host target gene.

BMPR1A BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BMPR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMPR1A BINDING SITE, designated SEQ ID:10528, to the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8680] Another function of VGAM90 is therefore inhibition of Bone Morphogenetic Protein Receptor, Type IA (BMPR1A, Accession NM_004329). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMPR1A. Endothelial Cell-specific Molecule 1 (ESM1, Accession NM_007036) is another VGAM90 host target gene. ESM1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ESM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESM1 BINDING SITE, designated SEQ ID:13911, to the nu-

cleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8681] Another function of VGAM90 is therefore inhibition of Endothelial Cell-specific Molecule 1 (ESM1, Accession NM_007036). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESM1. KIAA0408 (Accession NM_014702) is another VGAM90 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16234, to the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8682] Another function of VGAM90 is therefore inhibition of KIAA0408 (Accession NM_014702). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. LOC57117 (Accession NM_020395) is another VGAM90 host target gene. LOC57117 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC57117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57117 BINDING SITE, designated SEQ ID:21664, to the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8683] Another function of VGAM90 is therefore inhibition of LOC57117 (Accession NM_020395). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57117. LOC91585 (Accession XM_039395) is another VGAM90 host target gene. LOC91585 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91585, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91585 BINDING SITE, designated SEQ ID:33075, to the nucleotide sequence of VGAM90 RNA, herein designated VGAM RNA, also designated SEQ ID:2801.

[8684] Another function of VGAM90 is therefore inhibition of

LOC91585 (Accession XM_039395). Accordingly, utilities of VGAM90 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91585. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 91 (VGAM91) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8685] VGAM91 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM91 was detected is described hereinabove with reference to Figs. 1–8.

[8686] VGAM91 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8687] VGAM91 gene encodes a VGAM91 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM91 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM91 precursor RNA is designated SEQ ID:77, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:77 is located at position 20007 relative to the genome of *Plutella Xylostella Granulovirus*.

[8688] VGAM91 precursor RNA folds onto itself, forming VGAM91 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8689] An enzyme complex designated DICER COMPLEX, `dices` the VGAM91 folded precursor RNA into VGAM91 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide se-

quence of VGAM91 RNA is designated SEQ ID:2802, and is provided hereinbelow with reference to the sequence listing part.

[8690] VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM91 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[8691] VGAM91 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM91 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustrative

tion only, and is not meant to be limiting – VGAM91 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8692] The complementary binding of VGAM91 RNA, herein designated VGAM RNA, to host target binding sites on VGAM91 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM91 host target RNA into VGAM91 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8693] It is appreciated that VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM91 host target genes. The mRNA of each one of this plurality of VGAM91 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM91 RNA, herein designated VGAM RNA, and which when bound by VGAM91 RNA causes inhibition of translation of respective one or more VGAM91 host target proteins.

- [8694] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM91 gene, herein designated VGAM GENE, on one or more VGAM91 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).
- [8695] It is yet further appreciated that a function of VGAM91 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM91 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM91 correlate with, and may be deduced from, the identity of the host target genes which VGAM91 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8696] Nucleotide sequences of the VGAM91 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM91 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM91 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM91 are further described hereinbelow with reference to Table 1.

[8697] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM91 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM91 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8698] As mentioned hereinabove with reference to Fig. 1, a function of VGAM91 gene, herein designated VGAM is in-

hibition of expression of VGAM91 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM91 correlate with, and may be deduced from, the identity of the target genes which VGAM91 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8699] Succinate Dehydrogenase Complex, Subunit D, Integral Membrane Protein (SDHD, Accession NM_003002) is a VGAM91 host target gene. SDHD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDHD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDHD BINDING SITE, designated SEQ ID:8898, to the nucleotide sequence of VGAM91 RNA, herein designated VGAM RNA, also designated SEQ ID:2802.

[8700] A function of VGAM91 is therefore inhibition of Succinate Dehydrogenase Complex, Subunit D, Integral Membrane Protein (SDHD, Accession NM_003002). Accordingly, utilities of VGAM91 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDHD. FLJ10324 (Accession NM_018059) is another

VGAM91 host target gene. FLJ10324 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10324, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10324 BINDING SITE, designated SEQ ID:19828, to the nucleotide sequence of VGAM91 RNA, herein designated VGAM RNA, also designated SEQ ID:2802.

[8701] Another function of VGAM91 is therefore inhibition of FLJ10324 (Accession NM_018059). Accordingly, utilities of VGAM91 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10324. LOC152876 (Accession XM_098279) is another VGAM91 host target gene. LOC152876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152876 BINDING SITE, designated SEQ ID:41560, to the nucleotide sequence of VGAM91 RNA, herein designated VGAM RNA, also designated SEQ ID:2802.

[8702] Another function of VGAM91 is therefore inhibition of LOC152876 (Accession XM_098279). Accordingly, utilities of VGAM91 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152876. LOC221749 (Accession XM_166341) is another VGAM91 host target gene. LOC221749 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221749, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221749 BINDING SITE, designated SEQ ID:44178, to the nucleotide sequence of VGAM91 RNA, herein designated VGAM RNA, also designated SEQ ID:2802.

[8703] Another function of VGAM91 is therefore inhibition of LOC221749 (Accession XM_166341). Accordingly, utilities of VGAM91 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221749. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 92 (VGAM92) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[8704] VGAM92 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM92 was detected is described hereinabove with reference to Figs. 1–8.

[8705] VGAM92 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8706] VGAM92 gene encodes a VGAM92 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM92 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM92 precursor RNA is designated SEQ ID:78, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:78 is located at position 54360 relative to the genome of Plutella Xylostella Granulovirus.

[8707] VGAM92 precursor RNA folds onto itself, forming VGAM92 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8708] An enzyme complex designated DICER COMPLEX, `dices` the VGAM92 folded precursor RNA into VGAM92 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM92 RNA is designated SEQ ID:2803, and is provided hereinbelow with reference to the sequence listing part.

[8709] VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM92 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8710] VGAM92 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM92 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM92 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[8711] The complementary binding of VGAM92 RNA, herein designated VGAM RNA, to host target binding sites on VGAM92 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM92 host target RNA into VGAM92 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8712] It is appreciated that VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM92 host target genes. The mRNA of each one of this plurality of VGAM92 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM92 RNA, herein designated VGAM RNA, and which when bound by VGAM92 RNA causes inhibition of translation of respective one or more VGAM92 host target proteins.

[8713] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM92 gene, herein designated VGAM GENE, on one or

more VGAM92 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8714] It is yet further appreciated that a function of VGAM92 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM92 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM92 correlate with, and may be deduced from, the identity of the host target genes which VGAM92 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8715] Nucleotide sequences of the VGAM92 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM92 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM92 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM92 are further de-
scribed hereinbelow with reference to Table 1.

[8716] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM92 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM92 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[8717] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM92 gene, herein designated VGAM is in-
hibition of expression of VGAM92 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM92 correlate with, and may be deduced from, the
identity of the target genes which VGAM92 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[8718] KIAA1045 (Accession XM_048592) is a VGAM92 host tar-
get gene. KIAA1045 BINDING SITE is HOST TARGET bind-

ing site found in the 3' untranslated region of mRNA encoded by KIAA1045, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1045 BINDING SITE, designated SEQ ID:35193, to the nucleotide sequence of VGAM92 RNA, herein designated VGAM RNA, also designated SEQ ID:2803.

[8719] A function of VGAM92 is therefore inhibition of KIAA1045 (Accession XM_048592). Accordingly, utilities of VGAM92 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1045. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 93 (VGAM93) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8720] VGAM93 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM93 was detected is described hereinabove with reference to Figs. 1-8.

[8721] VGAM93 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Plutella Xylostella Granulovirus. VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8722] VGAM93 gene encodes a VGAM93 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM93 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM93 precursor RNA is designated SEQ ID:79, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:79 is located at position 88464 relative to the genome of Plutella Xylostella Granulovirus.

[8723] VGAM93 precursor RNA folds onto itself, forming VGAM93 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8724] An enzyme complex designated DICER COMPLEX, `dices` the VGAM93 folded precursor RNA into VGAM93 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM93 RNA is designated SEQ ID:2804, and is provided hereinbelow with reference to the sequence listing part.

[8725] VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM93 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8726] VGAM93 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM93 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM93 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8727] The complementary binding of VGAM93 RNA, herein designated VGAM RNA, to host target binding sites on VGAM93 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM93 host target RNA into VGAM93 host target protein, herein design-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8728] It is appreciated that VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM93 host target genes. The mRNA of each one of this plurality of VGAM93 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM93 RNA, herein designated VGAM RNA, and which when bound by VGAM93 RNA causes inhibition of translation of respective one or more VGAM93 host target proteins.

[8729] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM93 gene, herein designated VGAM GENE, on one or more VGAM93 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8730] It is yet further appreciated that a function of VGAM93 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM93 correlate with, and may be deduced from, the identity of the host target genes which VGAM93 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8731] Nucleotide sequences of the VGAM93 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM93 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM93 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM93 are further described hereinbelow with reference to Table 1.

[8732] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM93 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM93 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8733] As mentioned hereinabove with reference to Fig. 1, a function of VGAM93 gene, herein designated VGAM is inhibition of expression of VGAM93 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM93 correlate with, and may be deduced from, the identity of the target genes which VGAM93 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8734] Carcinoembryonic Antigen-related Cell Adhesion Molecule 1 (biliary glycoprotein) (CEACAM1, Accession NM_001712) is a VGAM93 host target gene. CEACAM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEACAM1 BINDING SITE, designated SEQ ID:7440, to the nucleotide

sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8735] A function of VGAM93 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 1 (biliary glycoprotein) (CEACAM1, Accession NM_001712), a gene which is a major effector of VEGF and may be a target for the inhibition of tumor angiogenesis. Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM1. The function of CEACAM1 has been established by previous studies. Ergun et al. (2000) showed that CEACAM1 exhibits angiogenic properties in in vitro and in vivo angiogenesis assays. CEACAM1 purified from granulocytes and endothelial cell media as well as recombinant CEACAM1 expressed in HEK293 cells stimulated proliferation, chemotaxis, and capillary-like tube formation of human microvascular endothelial cells. They increased vascularization of chick chorioallantoic membrane and potentiated the effects of VEGF165 (OMIM Ref. No. 192240). VEGF165 increased CEACAM1 expression at both the mRNA and the protein level. VEGF165-induced endothelial tube formation was blocked by a monoclonal CEACAM1 antibody. These data sug-

gested that CEACAM1 is a major effector of VEGF in the early microvessel formation. Since CEACAM1 is expressed in tumor microvessels but not in large blood vessels, CEACAM1 may be a target for the inhibition of tumor angiogenesis. Following infection with *Neisseria gonorrhoea*, there is a transient decline in circulating CD4 (OMIM Ref. No. 186940)-positive T lymphocytes that resolves after bacterial clearance. The gonococcus adheres to and is taken up by host cells through opacity-associated (Opa) proteins. Some Opa variants bind to heparan sulfate proteoglycans (HSPGs, e.g., SDC2; 142460), while others are specific for members of the CEACAM1/CD66 receptor family. CEACAM1 is the only member of this family that is expressed by lymphocytes and that contains a cytoplasmic ITIM (immunoreceptor tyrosine-based inhibitory motif). Using flow cytometry, Boulton and Gray-Owen (2002) demonstrated that CEACAM1 expression is upregulated after lymphocyte activation. Exposure to gonococci expressing the HSPG-specific Opa50 protein increased and exposure to CEACAM1-specific Opa52 gonococci or to anti-CEACAM1 antibody inhibited expression of the CD69 (OMIM Ref. No. 107273) activation marker on and proliferation by lymphocytes stimulated in vitro. The reduction

in lymphocyte proliferation was not due to an increase in cell death. CEACAM1 associated with Opa52 also interacted with SHP1 (OMIM Ref. No. 176883) and SHP2 (OMIM Ref. No. 176876), presumably through its cytoplasmic ITIM. Boulton and Gray-Owen (2002) suggested that Opa52 engagement of the CEACAM1 coinhibitory receptor induces immunosuppression and may explain the failure of the host to develop a memory humoral response to N. gonorrhea infection due to a lack of T-cell help for B-cell activation. Animal model experiments lend further support to the function of CEACAM1. Poy et al. (2002) hypothesized that insulin stimulates phosphorylation of CEACAM1 which in turn leads to upregulation of receptor-mediated insulin endocytosis and degradation in the hepatocyte. To test the hypothesis, they generated transgenic mice overexpressing in liver a dominant-negative phosphorylation-defective CEACAM1 mutant, S503A. Supporting their hypothesis, they found that S503A-CEACAM1 transgenic mice developed hyperinsulinemia resulting from impaired insulin clearance. The hyperinsulinemia caused secondary insulin resistance with impaired glucose tolerance and random, but not fasting, hyperglycemia. Transgenic mice developed visceral adiposity with in-

creased amounts of plasma free fatty acids and plasma and hepatic triglycerides. These findings suggested a mechanism through which insulin signaling regulates insulin sensitivity by modulating hepatic insulin clearance.

[8736] It is appreciated that the abovementioned animal model for CEACAM1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[8737] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8738] Ergun, S.; Kilic, N.; Ziegeler, G.; Hansen, A.; Nollau, P.; Gotze, J.; Wurmbach, J.-H.; Horst, A.; Weil, J.; Fernando, M.; Wagener, C. : CEA-related cell adhesion molecule 1: a potent angiogenic factor and a major effector of vascular endothelial growth factor. *Molec. Cell* 5: 311-320, 2000. ; and

[8739] Boulton, I. C.; Gray-Owen, S. D. : Neisserial binding to CEACAM1 arrests the activation and proliferation of CD4+ T lymphocytes. *Nature Immun.* 3: 229-236, 2002.

[8740] Further studies establishing the function and utilities of CEACAM1 are found in John Hopkins OMIM database record ID 109770, and in sited publications numbered

12145, 12146, 12147–12149, 10742, 12150–12151, 221, 10739–10740, 10743, 1215 and 10744 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Endometrial Bleeding Associated Factor (left–right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM_037302) is another VGAM93 host target gene. EBAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EBAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EBAF BINDING SITE, designated SEQ ID:32607, to the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8741] Another function of VGAM93 is therefore inhibition of Endometrial Bleeding Associated Factor (left–right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM_037302), a gene which LEFT–RIGHT AXIS MALFORMATIONS. Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EBAF. The function of EBAF has been established by previous studies.

Because of the possibility that Lefty mutations may be associated with human L–R axis malformations, Kosaki et al. (1999) characterized 2 human homologs, LEFTY A and LEFTY B (OMIM Ref. No. 603037). PCR screening of a PAC genomic library identified a clone that contained both LEFTY A and LEFTY B genes. Restriction mapping showed that the genes are separated by approximately 50 kb and are oriented in tandem. The 2 genes were localized by FISH to 1q42, a region syntenic to the location to which the mouse Lefty genes have been mapped at 1H5 (Meno et al., 1997). Both LEFTY A and LEFTY B contain 4 exons which are spliced at identical positions, and both genes encode proteins with 366 amino acids. LEFTY A was found to be identical to EBAF, the cDNA previously identified by Kothapalli et al. (1997). The deduced amino acid sequences of LEFTY A and LEFTY B are more similar to each other than to Lefty–1 or Lefty–2 of the mouse. Analysis of 126 human cases of L–R axis malformation showed 1 nonsense and 1 missense mutation in the LEFTY A gene. Both mutations lay in the cysteine–knot region of the LEFTY A protein, and the phenotype of affected individuals was very similar to that typically seen in Lefty–1 –/– mice with L–R axis malformations. Because of the possibility

that Lefty mutations may be associated with human L–R axis malformations, Kosaki et al. (1999) characterized 2 human homologs, LEFTY A and LEFTY B (OMIM Ref. No. 603037). PCR screening of a PAC genomic library identified a clone that contained both LEFTY A and LEFTY B genes. Restriction mapping showed that the genes are separated by approximately 50 kb and are oriented in tandem. The 2 genes were localized by FISH to 1q42, a region syntenic to the location to which the mouse Lefty genes have been mapped at 1H5 (Meno et al., 1997). Both LEFTY A and LEFTY B contain 4 exons which are spliced at identical positions, and both genes encode proteins with 366 amino acids. LEFTY A was found to be identical to EBAF, the cDNA previously identified by Kothapalli et al. (1997). The deduced amino acid sequences of LEFTY A and LEFTY B are more similar to each other than to Lefty–1 or Lefty–2 of the mouse. Analysis of 126 human cases of L–R axis malformation showed 1 nonsense and 1 missense mutation in the LEFTY A gene. Both mutations lay in the cysteine–knot region of the LEFTY A protein, and the phenotype of affected individuals was very similar to that typically seen in Lefty–1 –/– mice with L–R axis malformations. Animal model experiments lend further support to

the function of EBAF. Lefty-1, lefty-2, and nodal (OMIM Ref. No. 601265) are expressed on the left side of developing mouse embryos and are implicated in L-R determination. Meno et al. (1998) examined the role of lefty-1 by analyzing mutant mice lacking this gene. The lefty-1-deficient mice showed a variety of L-R positional defects in visceral organs. The most common feature of lefty-1 -/- mice was thoracic left isomerism (rather than right isomerism). The lack of lefty-1 resulted in bilateral expression of nodal, lefty-2, and Pitx2 (OMIM Ref. No. 601542), a homeo box gene normally expressed on the left side. These observations suggested that the role of lefty-1 is to restrict the expression of lefty-2 and nodal to the left side, and that lefty-2 or nodal encode a signal for 'leftness.'

[8742] It is appreciated that the abovementioned animal model for EBAF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8743] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8744] Kosaki, K.; Bassi, M. T.; Kosaki, R.; Lewin, M.; Belmont, J.;

Schauer, G.; Casey, B. : Characterization and mutation analysis of human LEFTY A and LEFTY B, homologues of murine genes implicated in left-right axis development. Am. J. Hum. Genet. 64: 712-721, 1999. ; and

[8745] Meno, C.; Shimonio, A.; Saijoh, Y.; Yashiro, K.; Mochida, K.; Ohishi, S.; Noji, S.; Kondoh, H.; Hamada, H. : Lefty-1 is required for left-right determination as a regulator of lefty-2 an.

[8746] Further studies establishing the function and utilities of EBAF are found in John Hopkins OMIM database record ID 601877, and in cited publications numbered 11847-1299 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Notch Homolog 2 (Drosophila) (NOTCH2, Accession NM_024408) is another VGAM93 host target gene. NOTCH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NOTCH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOTCH2 BINDING SITE, designated SEQ ID:23648, to the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8747] Another function of VGAM93 is therefore inhibition of Notch Homolog 2 (*Drosophila*) (NOTCH2, Accession NM_024408), a gene which is moderately similar to a region of murine Notch1 and contains an ankyrin repeat. Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOTCH2. The function of NOTCH2 has been established by previous studies. In *Drosophila*, the 'Notch' gene controls differentiation to various cell fates in many tissues. Three mammalian 'Notch' homologs have been identified. All 3 are very highly conserved relative to the *Drosophila* gene, which suggests that they are important for cell differentiation in mammals. This notion is supported by the previous finding of a truncated, translocated form of the human NOTCH1 (OMIM Ref. No. 190198) gene (formerly TAN1) in 3 cases of leukemia. Larsson et al. (1994) identified cosmid clones for all 3 human NOTCH genes. Using these clones as probes in fluorescence in situ hybridization to human metaphase chromosomes, they obtained results which, combined with data from somatic cell hybrid panels, demonstrated that NOTCH2 is located on 1p13-p11 and NOTCH3 on 19p13.2-p13.1, which are regions of neoplasia-associ-

ated translocation. As part of a study of a triplication of several Mb occurring on chromosomes 1, 6, and 9, Katsanis et al. (1996) confirmed the presence of a NOTCH locus on chromosome 1. Gao et al. (1998) mapped the mouse Notch2 gene to chromosome 3.

[8748] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8749] Katsanis, N.; Fitzgibbon, J.; Fisher, E. M. C. : Paralogy mapping: identification of a region in the human MHC triplicated onto human chromosomes 1 and 9 allows the prediction and isolation of novel PBX and NOTCH loci. Genomics 35: 101–108, 1996. ; and

[8750] Larsson, C.; Lardelli, M.; White, I.; Lendahl, U. : The human NOTCH1, 2, and 3 genes are located at chromosome positions 9q34, 1p13–p11, and 19p13.2–p13.1 in regions of neoplasia–associa.

[8751] Further studies establishing the function and utilities of NOTCH2 are found in John Hopkins OMIM database record ID 600275, and in cited publications numbered 841 and 10369 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0232 (Accession XM_052627) is another

VGAM93 host target gene. KIAA0232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0232 BINDING SITE, designated SEQ ID:36034, to the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8752] Another function of VGAM93 is therefore inhibition of KIAA0232 (Accession XM_052627). Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0232. TU12B1-TY (Accession NM_016575) is another VGAM93 host target gene. TU12B1-TY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TU12B1-TY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TU12B1-TY BINDING SITE, designated SEQ ID:18645, to the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8753] Another function of VGAM93 is therefore inhibition of TU12B1-TY (Accession NM_016575). Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TU12B1-TY. LOC90786 (Accession XM_034127) is another VGAM93 host target gene. LOC90786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90786 BINDING SITE, designated SEQ ID:32012, to the nucleotide sequence of VGAM93 RNA, herein designated VGAM RNA, also designated SEQ ID:2804.

[8754] Another function of VGAM93 is therefore inhibition of LOC90786 (Accession XM_034127). Accordingly, utilities of VGAM93 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90786. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 94 (VGAM94) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[8755] VGAM94 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM94 was detected is described hereinabove with reference to Figs. 1–8.

[8756] VGAM94 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8757] VGAM94 gene encodes a VGAM94 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM94 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM94 precursor RNA is designated SEQ ID:80, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:80 is located at position 54184 relative to the genome of Plutella Xylostella Granulovirus.

[8758] VGAM94 precursor RNA folds onto itself, forming VGAM94 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8759] An enzyme complex designated DICER COMPLEX, `dices` the VGAM94 folded precursor RNA into VGAM94 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM94 RNA is designated SEQ ID:2805, and is provided hereinbelow with reference to the sequence listing part.

[8760] VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM94 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8761] VGAM94 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM94 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM94 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[8762] The complementary binding of VGAM94 RNA, herein designated VGAM RNA, to host target binding sites on VGAM94 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM94 host target RNA into VGAM94 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8763] It is appreciated that VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM94 host target genes. The mRNA of each one of this plurality of VGAM94 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM94 RNA, herein designated VGAM RNA, and which when bound by VGAM94 RNA causes inhibition of translation of respective one or more VGAM94 host target proteins.

[8764] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM94 gene, herein designated VGAM GENE, on one or

more VGAM94 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8765] It is yet further appreciated that a function of VGAM94 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM94 correlate with, and may be deduced from, the identity of the host target genes which VGAM94 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8766] Nucleotide sequences of the VGAM94 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM94 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM94 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM94 are further de-
scribed hereinbelow with reference to Table 1.

[8767] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM94 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM94 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[8768] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM94 gene, herein designated VGAM is in-
hibition of expression of VGAM94 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM94 correlate with, and may be deduced from, the
identity of the target genes which VGAM94 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[8769] BLAME (Accession NM_020125) is a VGAM94 host target
gene. BLAME BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by BLAME, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLAME BINDING SITE, designated SEQ ID:21309, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8770] A function of VGAM94 is therefore inhibition of BLAME (Accession NM_020125). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLAME. Chromosome 10 Open Reading Frame 2 (C10orf2, Accession NM_021830) is another VGAM94 host target gene. C10orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C10orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C10orf2 BINDING SITE, designated SEQ ID:22403, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8771] Another function of VGAM94 is therefore inhibition of Chromosome 10 Open Reading Frame 2 (C10orf2, Accession NM_021830). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C10orf2. Calcitonin Receptor (CALCR, Accession NM_001742) is another VGAM94 host target gene. CALCR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALCR BINDING SITE, designated SEQ ID:7478, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8772] Another function of VGAM94 is therefore inhibition of Calcitonin Receptor (CALCR, Accession NM_001742), a gene which is a receptor for calcitonin, is mediated by G proteins which activate adenylyl cyclase, and thought to couple to the heterotrimeric guanosine triphosphate-binding protein that is sensitive to cholera toxin. Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CALCR. The function of CALCR has been established by previous studies. Taboulet et al. (1996) had reported the point mutation polymorphism (OMIM Ref. No. T to C) in the 3-prime region of the CALCR gene which induced a pro447-to-leu amino acid change in the third intracellular domain of the protein. This was the same mutation as that subsequently identified by Nakamura et al. (1997) and Masi et al. (1998) and referred to as pro463 to leu; the difference in numbering depended on whether isoform 1 or isoform 2 of the calcitonin receptor, with or without the 16-amino acid insert, was referred to (de Vernejoul, 1999). Taboulet et al. (1998) studied the distribution of these alleles in a cohort of 123 women with no osteoporotic fractures and 92 women who presented with one or more osteoporotic fractures of wrist or vertebrae. They found that bone mineral density of the femoral neck was significantly higher in heterozygous subjects compared with the homozygous leucine and homozygous proline genotypes. Also, a decreased fracture risk was observed in heterozygote subjects. In conclusion, they suggested that polymorphism of CALCR is associated with osteoporotic factors and bone mineral density in a population of post-menopausal women. The heterozygous advantage of the

pro/leu subjects could explain their protection against osteoporosis. The distribution of the CALCR alleles in the French population studied by Taboulet et al. (1998) was quite different from that observed by Nakamura et al. (1997) in the Japanese population. In Japan, the proline homozygote was the most frequent genotype (70%), Gorn et al. (1992) cloned a human calcitonin receptor cDNA from a eukaryotic expression library prepared from an ovarian small cell carcinoma cell line. A cell line had been shown to respond to calcitonin (CT, or CALCA; 114130) with increases in content of cellular cAMP. Transfection of this cDNA into COS cells resulted in expression of receptors with high affinity for salmon and human calcitonin. The expressed CALCR was coupled to adenylate cyclase. Northern analysis indicated a single transcript of about 4.2 kb. The cloned cDNA encoded a putative peptide of 490 amino acids with 7 potential transmembrane domains. The amino acid sequence was 73% identical to porcine CALCR, although the human CALCR contained an inset of 16 amino acids between transmembrane domains I and II. CALCR is closely related to the parathyroid hormone receptor (OMIM Ref. No. 168468) and the secretin receptor (OMIM Ref. No. 182098); these receptors com-

prise a distinct family of G protein-coupled 7-transmembrane domain receptors. A comparison of the human CALCR sequence to protein sequences in databases suggested that the receptor for calcitonin is evolutionarily related to the chemoattractant receptor of the primitive eukaryote *Dictyostelium discoideum*.

[8773] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8774] Gorn, A. H.; Lin, H. Y.; Yamin, M.; Auron, P. E.; Flannery, M. R.; Tapp, D. R.; Manning, C. A.; Lodish, H. F.; Krane, S. M.; Goldring, S. R. : Cloning, characterization, and expression of a human calcitonin receptor from an ovarian carcinoma cell line. *J. Clin. Invest.* 90: 1726-1735, 1992. ; and

[8775] Taboulet, J.; Frenkian, M.; Frendo, J. L.; Feingold, N.; Jullienne, A.; de Vernejoul, M. C. : Calcitonin receptor polymorphism is associated with a decreased fracture risk in post-menop.

[8776] Further studies establishing the function and utilities of CALCR are found in John Hopkins OMIM database record ID 114131, and in cited publications numbered 2336-2338, 3 and 12565-12570 listed in the bibliography section hereinbelow, which are also hereby incorpo-

rated by reference. Cytoplasmic Linker 2 (CYLN2, Accession NM_003388) is another VGAM94 host target gene. CYLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYLN2 BINDING SITE, designated SEQ ID:9421, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8777] Another function of VGAM94 is therefore inhibition of Cytoplasmic Linker 2 (CYLN2, Accession NM_003388), a gene which associates with microtubules and dendritic lamellar bodies. Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYLN2. The function of CYLN2 has been established by previous studies. Cytoplasmic linker proteins have been proposed to mediate the interaction between specific membranous organelles and microtubules. Hoogenraad et al. (1998) isolated and characterized overlapping murine and human cosmid clones respectively containing the complete mouse *Cyln2* gene,

which encodes cytoplasmic linker protein-115 (Clip-115), and the partial human CYLN2 gene. Based on nucleotide sequence comparisons and hybridization data, they concluded that the human CYLN2 gene includes the incomplete WBSCR4 and WBSCR3 transcription units identified by Osborne et al. (1996). Hoogenraad et al. (1998) found that the human CYLN2 gene spans at least 140 kb of DNA. The deduced partial human CYLN2 protein contains an N-terminal globular region with 2 microtubule-binding domains, followed by a potential alpha-helical coiled-coils region. Northern blot analysis with a rat Cyln2 cDNA probe detected a 5.5-kb CYLN2 message in human adult brain. Using a gene targeting approach, Hoogenraad et al. (2002) provided evidence that mice with haploinsufficiency for Cyln2 have features reminiscent of WBS, including mild growth deficiency, brain abnormalities, hippocampal dysfunction, and particular deficits in motor coordination. Absence of CLIP115 also leads to increased levels of CLIP170 (OMIM Ref. No. 179830), a closely related cytoplasmic linker protein, and dynactin (DCTN1; 601143) at the tips of growing microtubules. This protein redistribution may affect dynein motor regulation and, together with the loss of CLIP115-specific functions, under-

lie neurologic alterations in WBS.

[8778] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8779] Hoogenraad, C. C.; Koekkoek, B.; Akhmanova, A.; Krugers, H.; Dortland, B.; Miedema, M.; van Alphen, A.; Kistler, W. M.; Jaegle, M.; Koutsourakis, M.; Van Camp, N.; Verhoye, M.; van der Linden, A.; Kaverina, I.; Grosveld, F.; De Zeeuw, C. I.; Galjart, N. : Targeted mutation of Cyln2 in the Williams syndrome critical region links CLIP-115 haploinsufficiency to neurodevelopmental abnormalities in mice. Nature Genet. 32: 116-127, 2002. Note: Erratum: Nature Genet. 32: 331 only, 2002. ; and

[8780] Osborne, L. R.; Martindale, D.; Scherer, S. W.; Shi, X.-M.; Huizenga, J.; Heng, H. H. Q.; Costa, T.; Pober, B.; Lew, L.; Brinkman, J.; Rommens, J.; Koop, B.; Tsui, L.-C. : Identification.

[8781] Further studies establishing the function and utilities of CYLN2 are found in John Hopkins OMIM database record ID 603432, and in cited publications numbered 5347, 998 and 10456 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Eukaryotic Translation Initiation Factor 5A2 (EIF5A2,

Accession NM_020390) is another VGAM94 host target gene. EIF5A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF5A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5A2 BINDING SITE, designated SEQ ID:21660, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8782] Another function of VGAM94 is therefore inhibition of Eukaryotic Translation Initiation Factor 5A2 (EIF5A2, Accession NM_020390). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5A2. Zuo1in Related Factor 1 (ZRF1, Accession XM_168590) is another VGAM94 host target gene. ZRF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZRF1 BINDING SITE, designated SEQ ID:45267, to the nucleotide sequence of

VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8783] Another function of VGAM94 is therefore inhibition of Zuotin Related Factor 1 (ZRF1, Accession XM_168590). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZRF1. Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM_019034) is another VGAM94 host target gene. ARHF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHF BINDING SITE, designated SEQ ID:21121, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8784] Another function of VGAM94 is therefore inhibition of Ras Homolog Gene Family, Member F (in filopodia) (ARHF, Accession NM_019034). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHF. FLJ13110 (Accession NM_022912) is another VGAM94 host target

gene. FLJ13110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13110 BINDING SITE, designated SEQ ID:23220, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8785] Another function of VGAM94 is therefore inhibition of FLJ13110 (Accession NM_022912). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13110. FLJ14146 (Accession NM_024709) is another VGAM94 host target gene. FLJ14146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14146 BINDING SITE, designated SEQ ID:24034, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8786] Another function of VGAM94 is therefore inhibition of FLJ14146 (Accession NM_024709). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14146. KIAA0169 (Accession XM_052725) is another VGAM94 host target gene. KIAA0169 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0169 BINDING SITE, designated SEQ ID:36053, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8787] Another function of VGAM94 is therefore inhibition of KIAA0169 (Accession XM_052725). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0169. KIAA0864 (Accession XM_032630) is another VGAM94 host target gene. KIAA0864 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0864, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0864 BINDING SITE, designated SEQ ID:31684, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8788] Another function of VGAM94 is therefore inhibition of KIAA0864 (Accession XM_032630). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0864. MGC15705 (Accession NM_032757) is another VGAM94 host target gene. MGC15705 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15705 BINDING SITE, designated SEQ ID:26500, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8789] Another function of VGAM94 is therefore inhibition of MGC15705 (Accession NM_032757). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC15705. p25 (Accession NM_007030) is another VGAM94 host target gene. p25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by p25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of p25 BINDING SITE, designated SEQ ID:13892, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8790] Another function of VGAM94 is therefore inhibition of p25 (Accession NM_007030). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with p25. Phytoceramide, Alkaline (PHCA, Accession NM_018367) is another VGAM94 host target gene. PHCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHCA BINDING SITE, designated SEQ ID:20376, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2805.

[8791] Another function of VGAM94 is therefore inhibition of Phytoceramidase, Alkaline (PHCA, Accession NM_018367). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHCA. Protein-O-mannosyltransferase 1 (POMT1, Accession NM_007171) is another VGAM94 host target gene. POMT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POMT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POMT1 BINDING SITE, designated SEQ ID:14018, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8792] Another function of VGAM94 is therefore inhibition of Protein-O-mannosyltransferase 1 (POMT1, Accession NM_007171). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POMT1. LOC152925 (Accession XM_087559) is another VGAM94 host target gene. LOC152925 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LOC152925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152925 BINDING SITE, designated SEQ ID:39335, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8793] Another function of VGAM94 is therefore inhibition of LOC152925 (Accession XM_087559). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152925. LOC221463 (Accession XM_166374) is another VGAM94 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44201, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8794] Another function of VGAM94 is therefore inhibition of

LOC221463 (Accession XM_166374). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221463. LOC254266 (Accession XM_173221) is another VGAM94 host target gene. LOC254266 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254266, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254266 BINDING SITE, designated SEQ ID:46481, to the nucleotide sequence of VGAM94 RNA, herein designated VGAM RNA, also designated SEQ ID:2805.

[8795] Another function of VGAM94 is therefore inhibition of LOC254266 (Accession XM_173221). Accordingly, utilities of VGAM94 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254266. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 95 (VGAM95) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[8796] VGAM95 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM95 was detected is described hereinabove with reference to Figs. 1–8.

[8797] VGAM95 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8798] VGAM95 gene encodes a VGAM95 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM95 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM95 precursor RNA is designated SEQ ID:81, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:81 is located at position 13652 relative to the genome of Plutella Xylostella Granulovirus.

[8799] VGAM95 precursor RNA folds onto itself, forming VGAM95 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin

structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8800] An enzyme complex designated DICER COMPLEX, `dices` the VGAM95 folded precursor RNA into VGAM95 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM95 RNA is designated SEQ ID:2806, and is provided hereinbelow with reference to the sequence listing part.

[8801] VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM95 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3`

untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8802] VGAM95 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM95 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM95 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8803] The complementary binding of VGAM95 RNA, herein designated VGAM RNA, to host target binding sites on VGAM95 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM95 host target RNA into VGAM95 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8804] It is appreciated that VGAM95 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM95 host target genes. The mRNA of each one of this plurality of VGAM95 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM95 RNA, herein designated VGAM RNA, and which when bound by VGAM95 RNA causes inhibition of translation of respective one or more VGAM95 host target proteins.

[8805] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM95 gene, herein designated VGAM GENE, on one or more VGAM95 host target gene, herein designated VGAM

HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8806] It is yet further appreciated that a function of VGAM95 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM95 correlate with, and may be deduced from, the identity of the host target genes which VGAM95 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8807] Nucleotide sequences of the VGAM95 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM95 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM95 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM95 are further described hereinbelow with reference to Table 1.

[8808] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM95 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM95 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8809] As mentioned hereinabove with reference to Fig. 1, a function of VGAM95 gene, herein designated VGAM is inhibition of expression of VGAM95 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM95 correlate with, and may be deduced from, the identity of the target genes which VGAM95 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8810] Calcium Channel, Voltage-dependent, Beta 2 Subunit (CACNB2, Accession NM_000724) is a VGAM95 host target gene. CACNB2 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by CACNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNB2 BINDING SITE, designated SEQ ID:6388, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8811] A function of VGAM95 is therefore inhibition of Calcium Channel, Voltage-dependent, Beta 2 Subunit (CACNB2, Accession NM_000724). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNB2.

CD2-associated Protein (CD2AP, Accession NM_012120) is another VGAM95 host target gene. CD2AP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CD2AP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD2AP BINDING SITE, designated SEQ ID:14434, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8812] Another function of VGAM95 is therefore inhibition of CD2-associated Protein (CD2AP, Accession NM_012120), a gene which binds CAS ligand and may therefore involve in its growth regulatory pathway. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD2AP. The function of CD2AP has been established by previous studies. P130(Cas) (OMIM Ref. No. 602941) is a docking protein that is tyrosine-phosphorylated in response to a variety of extracellular stimuli, such as growth factors, cell-cell interaction, and cell-matrix interaction, and appears to play a critical role in the integrin-linked formation of focal complexes. To understand the growth regulatory pathway of p130(Cas), Kirsch et al. (1999) used the yeast 2-hybrid system to search for interacting molecules. They identified a human protein, which they called CMS for p130(Cas) ligand with multiple SH3 domains, as a direct binding protein of p130(Cas). CMS is a multifunctional adapter-type molecule, which is localized in the cytoplasm, membrane ruffles, and leading edges of cells. Its structure and colocalization with F-actin (see OMIM Ref. No. 102610) and p130(Cas) suggested a function as a scaffolding protein involved in the dynamic regulation of

the actin cytoskeleton. The cDNA corresponding to CMS encodes a protein of 639 amino acids with a deduced molecular mass of approximately 70 kD. Amino acid analysis revealed that CMS contains in its N terminus 3 SH3 domains followed by a proline-rich region containing binding sites for SH3 domains. Putative actin-binding sites and a coiled-coil domain are located at the C terminus of the protein, which also contains a putative leucine zipper motif. CMS mRNA is ubiquitously expressed in adult and fetal human tissues as an approximately 5.4-kb transcript, as detected by Northern blot analysis. CMS induces vesicle formation and colocalizes with p130(Cas) and F-actin to membrane ruffles. It also associates with and is phosphorylated by tyrosine kinases. Kirsch et al. (1999) demonstrated that CMS is able to homodimerize through the coiled-coil domain located in its C terminus. There was no evidence for intermolecular or intramolecular binding via the SH3 domains and PXXP binding. Animal model experiments lend further support to the function of CD2AP. Shih et al. (1999) generated mice lacking CD2AP by targeted disruption. In CD2AP-deficient mice, immune function was compromised, but the mice died from renal failure at 6 to 7 weeks of age. In the kidney, CD2AP was

expressed primarily in glomerular epithelial cells. Knock-out mice exhibited defects in epithelial cell foot processes, accompanied by mesangial cell hyperplasia and extracellular matrix deposition. CD2AP associated with nephrin (OMIM Ref. No. 602716), which is the primary component of the slit diaphragm. This observation supports a role for CD2AP in this specialized cell junction.

[8813] It is appreciated that the abovementioned animal model for CD2AP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8814] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8815] Kirsch, K. H.; Georgescu, M.-M.; Ishimaru, S.; Hanafusa, H. : CMS: an adapter molecule involved in cytoskeletal rearrangements. Proc. Nat. Acad. Sci. 96: 6211-6216, 1999. ; and

[8816] Shih, N.-Y.; Li, J.; Karpitskii, V.; Nguyen, A.; Dustin, M. L.; Kanagawa, O.; Miner, J. H.; Shaw, A. S. : Congenital nephrotic syndrome in mice lacking CD2-associated protein. Science 2.

[8817] Further studies establishing the function and utilities of

CD2AP are found in John Hopkins OMIM database record ID 604241, and in cited publications numbered 5273–5275 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Exostoses (multiple)–like 3 (EXTL3, Accession NM_001440) is another VGAM95 host target gene. EXTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EXTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EXTL3 BINDING SITE, designated SEQ ID:7168, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8818] Another function of VGAM95 is therefore inhibition of Exostoses (multiple)–like 3 (EXTL3, Accession NM_001440), a gene which is a member of the multiple exostoses gene family. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EXTL3. The function of EXTL3 has been established by previous studies. By EST database searching with the sequences of EXT1 (OMIM Ref. No. 133700), EXT2 (OMIM Ref. No. 133701), and EXTL1 (OMIM

Ref. No. 601738), followed by 5-prime and 3-prime RACE, Saito et al. (1998) cloned full-length cDNAs for 2 new members of the EXT family, EXTL2 (OMIM Ref. No. 602411) and EXTL3, which they called EXTR2 and EXTR1, respectively. The deduced 919-amino acid EXTL3 protein contains a highly conserved region in the C terminus common to other EXT proteins. Northern blot analysis detected expression of 6.2- and 4.7-kb EXTR1 transcripts in all tissues tested except ovary. The larger transcript was predominant in brain, skeletal muscle, and testis, and the shorter transcript in heart, liver, thymus, and prostate. Kobayashi et al. (2000) isolated a cDNA for a REG protein (see OMIM Ref. No. 167770) receptor from a rat islet cDNA library. Cells into which the cDNA had been introduced bound REG protein with high affinity. When the cDNA was introduced into a pancreatic beta-cell line that showed REG-dependent growth, the transformants exhibited a significant increase in the incorporation of 5-prime-bromo-2-prime-deoxyuridine as well as in the cell numbers in response to REG protein. A homology search revealed that the rat REG protein receptor cDNA is a homolog of EXTL3. The rat and human proteins share 97% sequence identity. Kobayashi et al. (2000) found that

REG receptor mRNA in the rat is detectable in liver, kidney, stomach, small intestine, colon, adrenal gland, pituitary gland, and brain, but not in heart, suggesting the possible involvement of the REG-REG protein receptor signal system in a variety of cell types other than pancreatic beta cells. By somatic cell hybrid and radiation hybrid analyses, Saito et al. (1998) mapped the human EXTL3 gene to chromosome 8p21. By FISH, radiation hybrid analysis, and inclusion within a mapped contig, Van Hul et al. (1998) mapped the gene to 8p21-p12.

- [8819] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8820] Saito, T.; Seki, N.; Yamauchi, M.; Tsuji, S.; Hayashi, A.; Kozuma, S.; Hori, T. : Structure, chromosomal location, and expression profile of EXTR1 and EXTR2, new members of the multiple exostoses gene family. *Biochem. Biophys. Res. Commun.* 243: 61-66, 1998. ; and
- [8821] Van Hul, W.; Wuyts, W.; Hendrickx, J.; Speleman, F.; Wauters, J.; De Boulle, K.; Van Roy, N.; Bossuyt, P.; Willems, P. J. : Identification of a third EXT-like gene (EXTL3) belonging to.
- [8822] Further studies establishing the function and utilities of

EXTL3 are found in John Hopkins OMIM database record ID 605744, and in cited publications numbered 450 and 6016 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Muscleblind-like (Drosophila) (MBNL, Accession NM_021038) is another VGAM95 host target gene. MBNL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MBNL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBNL BINDING SITE, designated SEQ ID:22029, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8823] Another function of VGAM95 is therefore inhibition of Muscleblind-like (Drosophila) (MBNL, Accession NM_021038), a gene which binds to cug triplet repeat expansion dsrna (by similarity). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBNL. The function of MBNL has been established by previous studies. By screening for cDNAs with the potential to encode large proteins expressed in brain, Ishikawa et al.

(1997) identified a cDNA encoding MBNL, which they designated KIAA0428. KIAA0428 encodes a deduced 370-amino acid protein. RT-PCR analysis detected highest expression of KIAA0428 in skeletal muscle, followed by prostate, lung, heart, small intestine, ovary, and placenta. Triplet repeat expansion disorders (e.g., myotonic dystrophy; 160900) are characterized by genetic anticipation in which disease severity is proportional and age-of-onset is inversely proportional to the size of the expansion mutation. By biochemical purification of HeLa cell proteins binding to dystrophin myotonia (DM1) protein kinase (DMPK; 605377) RNAs with variable numbers of CUG repeats, followed by peptide sequence analysis and PCR, Miller et al. (2000) isolated cDNAs encoding isoforms of MBNL, which they termed EXP. The 42- and 40-kD isoforms, EXP42 and EXP40, are identical to a previously identified 388-amino acid MBNL protein (GenBank CAA74155) and KIAA0428, respectively, while the 35-kD isoform, EXP35, is a novel 305-amino acid protein. Northern blot analysis revealed 6.5- and 5.3-kb EXP transcripts that were highly expressed in cardiac and skeletal muscle. Western blot analysis showed high expression of EXP42 in HeLa and lymphoblastoid cell lines. Immunofluorescence

microscopy demonstrated nuclear and cytoplasmic expression of EXP42 in normal myoblasts, while nuclear foci were enriched in DM1 myoblasts. FISH and immunofluorescence analyses suggested that DMPK mutant RNAs recruit and sequester EXP dsRNA-binding proteins. Miller et al. (2000) proposed that the DM1 mutation produces a competing dsRNA-binding substrate that recruits the EXP proteins and sequesters them away from their normal RNA-binding sites during cell differentiation. By radiation hybrid analysis, Ishikawa et al. (1997) mapped the MBNL gene to chromosome 3. Miller et al. (2000) mapped the MBNL gene to 3q25, distal to the DM2 (OMIM Ref. No. 602668) and PROMM (OMIM Ref. No. 600109) loci on 3q21.

[8824] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8825] Miller, J. W.; Urbinati, C. R.; Teng-umnuay, P.; Stenberg, M. G.; Byrne, B. J.; Thornton, C. A.; Swanson, M. S. : Recruitment of human muscleblind proteins to (CUG)_n expansions associated with myotonic dystrophy. EMBO J. 19: 4439–4448, 2000. ; and

[8826] Ishikawa, K.; Nagase, T.; Nakajima, D.; Seki, N.; Ohira, M.;

Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes.

[8827] Further studies establishing the function and utilities of MBNL are found in John Hopkins OMIM database record ID 606516, and in cited publications numbered 627 and 8760 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mannosyl (alpha-1,3-)-glycoprotein Beta-1,4-N-acetylglucosaminyltransferase, Isoenzyme B (MGAT4B, Accession NM_054013) is another VGAM95 host target gene. MGAT4B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGAT4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGAT4B BINDING SITE, designated SEQ ID:27621, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8828] Another function of VGAM95 is therefore inhibition of Mannosyl (alpha-1,3-)-glycoprotein Beta-1,4-N-acetylglucosaminyltransferase, Isoenzyme B

(MGAT4B, Accession NM_054013). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT4B. Non-POU Domain Containing, Octamer-binding (NONO, Accession XM_088688) is another VGAM95 host target gene. NONO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NONO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NONO BINDING SITE, designated SEQ ID:39900, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8829] Another function of VGAM95 is therefore inhibition of Non-POU Domain Containing, Octamer-binding (NONO, Accession XM_088688), a gene which is a nuclear protein which contains RNA recognition motifs. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NONO. The function of NONO has been established by previous studies. Dong et al. (1993) purified and cloned the cDNA of HeLa cell p54nrb, a nuclear protein with 2

RNA recognition motifs and extensive homology to human splicing factor PSF and *Drosophila* NONA/BJ6. Brown et al. (1997) examined the expression of 33 X-linked genes in 8 mouse/human somatic cell hybrids that contained either the human active (3 hybrids) or inactive (5 hybrids) X chromosome. They found that the p54nrb gene was expressed only in those hybrids with the active human X. Using a megabase scale from pter to qter devised by Nelson et al. (1995), they noted that the approximate physical position of the gene was 70 Mb from pter. Brown et al. (1997) placed it in almost exactly the same position as the CCG1 gene (TAF2A; 313650), which had been mapped to Xq13-q27, and approximately 2 Mb proximal to PHKA1 (OMIM Ref. No. 311870), which had been mapped to Xq13. Thus, Xq13 is the likely location. The AFX1 gene (OMIM Ref. No. 300033) and the NRB54 gene map to a yeast artificial chromosome (YAC) contig of Xq13.1 that harbors the X-linked dystonia-parkinsonism locus DYT3 (OMIM Ref. No. 314250). Peters et al. (1997) found that the AFX1 gene is composed of 3 exons with most of exon 3 being untranslated. The NRB54 gene is made up of 12 exons ranging in size from 40 to 1,227 bp. The start codon is in exon 3 and the stop codon in exon 12. Both

genes are expressed in the brain, among other tissues.

Peters et al. (1997) excluded both genes as candidates of DYT3 by sequencing of the exons and the flanking intronic sequences in a patient and a control, and by Northern blot analysis.

[8830] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8831] Brown, C. J.; Carrel, L.; Willard, H. F. : Expression of genes from the human active and inactive X chromosomes. *Am. J. Hum. Genet.* 60: 1333–1343, 1997. ; and

[8832] Peters, U.; Haberhausen, G.; Kostrzewa, M.; Nolte, D.; Muller, U. : AFX1 and p54(nrb): fine mapping, genomic structure, and exclusion as candidate genes of X-linked dystonia parkinsonism.

[8833] Further studies establishing the function and utilities of NONO are found in John Hopkins OMIM database record ID 300084, and in cited publications numbered 10974–1097 and 8709 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pim-1 Oncogene (PIM1, Accession XM_165800) is another VGAM95 host target gene. PIM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by PIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIM1 BINDING SITE, designated SEQ ID:43756, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8834] Another function of VGAM95 is therefore inhibition of Pim-1 Oncogene (PIM1, Accession XM_165800), a gene which is a protooncogene. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIM1. The function of PIM1 has been established by previous studies. Amson et al. (1989) showed that the 33-kD product of the PIM gene is highly expressed in the liver and spleen during fetal hematopoiesis. In contrast, it is only slightly expressed in circulating granulocytes in adults. It was over-expressed in hematopoietic malignancies, particularly in myeloid and lymphoid acute leukemias. The results implied a physiologic role of the PIM1 oncogene during hematopoietic development and a deregulation of the gene in various leukemias. Animal model experiments lend further support to the function of PIM1. To understand the

function of Pim1 and its role in hematopoietic development, Laird et al. (1993) generated mice deficient in Pim1 function. Pim1-deficient mice were ostensibly normal, healthy, and fertile; however, detailed analysis demonstrated a correlation of Pim1 deficiency with erythrocyte microcytosis, whereas overexpression of Pim1 in transgenic mice resulted in erythrocyte macrocytosis

[8835] It is appreciated that the abovementioned animal model for PIM1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8836] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8837] Laird, P. W.; van der Lugt, N. M. T.; Clarke, A.; Domen, J.; Linders, K.; McWhir, J.; Berns, A.; Hooper, M. : In vivo analysis of Pim-1 deficiency. *Nucleic Acids Res.* 21: 4750-4755, 1993. ; and

[8838] Amson, R.; Sigaux, F.; Przedborski, S.; Flandrin, G.; Givol, D.; Telerman, A. : The human protooncogene product p33pim is expressed during fetal hematopoiesis and in diverse leukemias. *Proc.*

[8839] Further studies establishing the function and utilities of

PIM1 are found in John Hopkins OMIM database record ID 164960, and in cited publications numbered 10810–10812, 1156 and 11115–11114 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Plasminogen Activator, Tissue (PLAT, Accession NM_000930) is another VGAM95 host target gene. PLAT BINDING SITE1 and PLAT BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PLAT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAT BINDING SITE1 and PLAT BINDING SITE2, designated SEQ ID:6638 and SEQ ID:26897 respectively, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8840] Another function of VGAM95 is therefore inhibition of Plasminogen Activator, Tissue (PLAT, Accession NM_000930). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAT. Reticulocalbin 2, EF-hand Calcium Binding Domain (RCN2, Accession NM_002902) is another VGAM95 host target gene. RCN2

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RCN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RCN2 BINDING SITE, designated SEQ ID:8805, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8841] Another function of VGAM95 is therefore inhibition of Reticulocalbin 2, EF-hand Calcium Binding Domain (RCN2, Accession NM_002902), a gene which binds calcium and interacts with papillomavirus E6 oncoprotein. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RCN2. The function of RCN2 has been established by previous studies. One major class of calcium-binding proteins is the EF-hand proteins, which includes calmodulin (see OMIM Ref. No. CALM1; 114180). Members of this family contain a helix-loop-helix motif, called the EF-hand, that coordinates calcium with high specificity. The endoplasmic reticulum (ER) is the major calcium storage compartment in nonmuscle eukaryotic cells. By screening a HeLa cell cDNA expression library with autoimmune

serum from a patient, Weis et al. (1994) cloned a human cDNA encoding an EF-hand protein, named RCN2. The predicted 317-amino acid RCN2 protein contains an N-terminal signal sequence, 6 copies of the EF-hand motif, and a C-terminal His-Asp-Glu-Leu (HDEL) sequence, which was originally defined as an ER retention motif in yeast proteins. Immunocytochemical localization and cell fractionation studies demonstrated that RCN2 is a resident ER protein; the HDEL motif is required for its ER retention. RCN2 was detected by antibodies in all cell lines tested. It binds calcium in vitro. By Western blotting, in vitro translated RCN2 protein has a molecular mass of 55 kD, leading the authors to designate it the 'endoplasmic reticulum calcium-binding protein of 55 kD' (ERC55). The RCN2 gene was assigned by a radiation hybrid panel to human chromosome 15, between D15S215 and D15S206 by Genethon, and between D15S114 and D15S1041 by the Stanford Human Genome Center (Schuler et al., 1996). By fluorescence in situ hybridization, Wang et al. (1997) mapped the RCN2 gene to 15q23. Because type 4 Bardet-Biedl syndrome (OMIM Ref. No. 600374) maps to this region, RCN2 may be implicated in the causation of that disorder.

- [8842] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8843] Weis, K.; Griffiths, G.; Lamond, A. I. : The endoplasmic reticulum calcium-binding protein of 55 kDa is a novel EF-hand protein retained in the endoplasmic reticulum by a carboxyl-terminal His-Asp-Glu-Leu motif. *J. Biol. Chem.* 269: 19142-19150, 1994. ; and
- [8844] Wang, J. Y.; Zhen, D. K.; Bianchi, D. W.; Androphy, E. J.; Chen, J. J. : Assignment of the gene for ERC-55 (RCN2) to human chromosome band 15q22.33-q24.1 by in situ hybridization. *Cytog.*
- [8845] Further studies establishing the function and utilities of RCN2 are found in John Hopkins OMIM database record ID 602584, and in cited publications numbered 9044-904 and 12708-9047 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TAR (HIV) RNA Binding Protein 2 (TARBP2, Accession NM_134324) is another VGAM95 host target gene. TARBP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TARBP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TARBP2 BINDING SITE, designated SEQ ID:28629, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8846] Another function of VGAM95 is therefore inhibition of TAR (HIV) RNA Binding Protein 2 (TARBP2, Accession NM_134324), a gene which is involved in the regulation of HIV replication. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TARBP2. The function of TARBP2 has been established by previous studies. By screening a HeLa cell cDNA library with a TAR RNA probe, Gatignol et al. (1991) purified a cDNA, TARBP2, encoding a 345-amino acid protein termed TRBP by the authors. Mutation analysis showed that the TARBP2 protein binds to the helix between the bulge and the loop of the TAR RNA. Functional analysis demonstrated that TARBP2 enhanced expression of the HIV-1 LTR 20- to 60-fold and that the transactivation required an intact TAR RNA structure. By sequence analysis, Kozak et al. (1995) determined that human and mouse TARBP2 genes are expressed as 1.6-kb transcripts. However, immunoblot analysis re-

vealed that TARBP2 encodes 90- and 37-kD proteins in mouse cells, a 37-kD protein in hamster cells, and a 55-kD protein in monkey and human cells.

[8847] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8848] Gatignol, A.; Buckler-White, A.; Berkhout, B.; Jeang, K. T. : Characterization of a human TAR RNA-binding protein that activates the HIV-1 LTR. *Science* 251: 1597-1600, 1991. ; and

[8849] Kozak, C. A.; Gatignol, A.; Graham, K.; Jeang, K. T.; McBride, O. W. : Genetic mapping in human and mouse of the locus encoding TRBP, a protein that binds the TAR region of the human i.

[8850] Further studies establishing the function and utilities of TARBP2 are found in John Hopkins OMIM database record ID 605053, and in cited publications numbered 5027-5029 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257) is another VGAM95 host target gene. TJP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TJP1, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TJP1 BINDING SITE, designated SEQ ID:9268, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8851] Another function of VGAM95 is therefore inhibition of Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257), a gene which colocalizes and interacts with cadherins in cells lacking tight junctions. Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TJP1. The function of TJP1 has been established by previous studies. Tight junction (zonula occludens) protein 1 (TJP1), also referred to as ZO-1, is a 200-kD protein located on a cytoplasmic membrane surface of vertebrate intercellular tight junctions. Willott et al. (1993) isolated a full-length cDNA sequence for human TJP1. Although the function of TJP1 is unknown, the cDNA sequence predicted a multi-domain signaling protein homologous to the product of the 'discs large-1' tumor suppressor gene of *Drosophila* (OMIM Ref. No. 601014) and several other membrane-associated proteins in mammals.

By fluorescence in situ hybridization using a cDNA probe, Mohandas et al. (1995) mapped TJP1 to 15q13. The Jackson Laboratory backcross DNA panel derived from interspecies crosses was used to map Tjp1 to mouse chromosome 7 in a region with conserved homology to 15q13. Fluorescence in situ hybridization studies on metaphases from patients with the Prader-Willi syndrome (OMIM Ref. No. 176270) and/or the Angelman syndrome (OMIM Ref. No. 105830) showed that TJP1 maps close but distal to the PWS/AS chromosome region.

[8852] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8853] Mohandas, T. K.; Chen, X.-N.; Rowe, L. B.; Birkenmeier, E. H.; Fanning, A. S.; Anderson, J. M.; Korenberg, J. R. : Localization of the tight junction protein gene TJP1 to human chromosome 15q13, distal to the Prader-Willi/Angelman region, and to mouse chromosome 7. *Genomics* 30: 594-597, 1995. ; and

[8854] Willott, E.; Balda, M. S.; Fanning, A. S.; Jameson, B.; Van Itallie, C.; Anderson, J. M. : The tight junction protein ZO-1 is homologous to the *Drosophila* discs-large tumor suppressor pr.

[8855] Further studies establishing the function and utilities of TJP1 are found in John Hopkins OMIM database record ID 601009, and in cited publications numbered 9454–9455 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM_015185) is another VGAM95 host target gene. ARHGEF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF9 BINDING SITE, designated SEQ ID:17542, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8856] Another function of VGAM95 is therefore inhibition of Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM_015185). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF9. BCMP1 (Accession NM_031442) is another VGAM95 host target gene. BCMP1 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by BCMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCMP1 BINDING SITE, designated SEQ ID:25457, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8857] Another function of VGAM95 is therefore inhibition of BCMP1 (Accession NM_031442). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCMP1. Calmegin (CLGN, Accession NM_004362) is another VGAM95 host target gene. CLGN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLGN BINDING SITE, designated SEQ ID:10570, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8858] Another function of VGAM95 is therefore inhibition of

Calmegin (CLGN, Accession NM_004362). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLGN. CMG2 (Accession NM_058172) is another VGAM95 host target gene. CMG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CMG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMG2 BINDING SITE, designated SEQ ID:27722, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8859] Another function of VGAM95 is therefore inhibition of CMG2 (Accession NM_058172). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMG2. DKFZP434E2318 (Accession NM_032138) is another VGAM95 host target gene. DKFZP434E2318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434E2318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of DKFZP434E2318 BINDING SITE, designated SEQ ID:25817, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8860] Another function of VGAM95 is therefore inhibition of DKFZP434E2318 (Accession NM_032138). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2318. DKFZp761D112 (Accession NM_032297) is another VGAM95 host target gene. DKFZp761D112 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D112 BINDING SITE, designated SEQ ID:26078, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8861] Another function of VGAM95 is therefore inhibition of DKFZp761D112 (Accession NM_032297). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

DKFZp761D112. FHR5 (Accession NM_030787) is another VGAM95 host target gene. FHR5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FHR5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHR5 BINDING SITE, designated SEQ ID:25086, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8862] Another function of VGAM95 is therefore inhibition of FHR5 (Accession NM_030787). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHR5. FLJ22390 (Accession NM_022746) is another VGAM95 host target gene. FLJ22390 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22390, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22390 BINDING SITE, designated SEQ ID:22959, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2806.

[8863] Another function of VGAM95 is therefore inhibition of FLJ22390 (Accession NM_022746). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22390. FLJ31153 (Accession NM_144600) is another VGAM95 host target gene. FLJ31153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31153 BINDING SITE, designated SEQ ID:29416, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8864] Another function of VGAM95 is therefore inhibition of FLJ31153 (Accession NM_144600). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31153. Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM_033327) is another VGAM95 host target gene. FUBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

FUBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUBP3 BINDING SITE, designated SEQ ID:31875, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8865] Another function of VGAM95 is therefore inhibition of Far Upstream Element (FUSE) Binding Protein 3 (FUBP3, Accession XM_033327). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUBP3. GTP Binding Protein 1 (GTPBP1, Accession NM_004286) is another VGAM95 host target gene. GTPBP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GTPBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTPBP1 BINDING SITE, designated SEQ ID:10498, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8866] Another function of VGAM95 is therefore inhibition of GTP

Binding Protein 1 (GTPBP1, Accession NM_004286). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTPBP1. KIAA0237 (Accession NM_014747) is another VGAM95 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16452, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8867] Another function of VGAM95 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0420 (Accession XM_032693) is another VGAM95 host target gene. KIAA0420 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0420, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0420 BINDING SITE, designated SEQ ID:31727, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8868] Another function of VGAM95 is therefore inhibition of KIAA0420 (Accession XM_032693). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0420. KIAA0483 (Accession NM_015176) is another VGAM95 host target gene. KIAA0483 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0483, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0483 BINDING SITE, designated SEQ ID:17530, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8869] Another function of VGAM95 is therefore inhibition of KIAA0483 (Accession NM_015176). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0483. KIAA0515 (Accession XM_033380) is another

VGAM95 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31927, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8870] Another function of VGAM95 is therefore inhibition of KIAA0515 (Accession XM_033380). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. KIAA0759 (Accession XM_041090) is another VGAM95 host target gene. KIAA0759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0759 BINDING SITE, designated SEQ ID:33443, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8871] Another function of VGAM95 is therefore inhibition of KIAA0759 (Accession XM_041090). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0759. KIAA1155 (Accession XM_030864) is another VGAM95 host target gene. KIAA1155 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1155 BINDING SITE, designated SEQ ID:31196, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8872] Another function of VGAM95 is therefore inhibition of KIAA1155 (Accession XM_030864). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1155. KIAA1449 (Accession NM_020839) is another VGAM95 host target gene. KIAA1449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1449, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1449 BINDING SITE, designated SEQ ID:21900, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8873] Another function of VGAM95 is therefore inhibition of KIAA1449 (Accession NM_020839). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1449. KIAA1656 (Accession XM_038022) is another VGAM95 host target gene. KIAA1656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1656 BINDING SITE, designated SEQ ID:32735, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8874] Another function of VGAM95 is therefore inhibition of KIAA1656 (Accession XM_038022). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1656. KIAA1735 (Accession XM_113686) is another VGAM95 host target gene. KIAA1735 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1735 BINDING SITE, designated SEQ ID:42346, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8875] Another function of VGAM95 is therefore inhibition of KIAA1735 (Accession XM_113686). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1735. KIAA1932 (Accession XM_055900) is another VGAM95 host target gene. KIAA1932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1932 BINDING SITE, designated SEQ ID:36349, to the nucleotide sequence of VGAM95 RNA, herein designated

VGAM RNA, also designated SEQ ID:2806.

[8876] Another function of VGAM95 is therefore inhibition of KIAA1932 (Accession XM_055900). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1932. MAN1 (Accession NM_014319) is another VGAM95 host target gene. MAN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1 BINDING SITE, designated SEQ ID:15618, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8877] Another function of VGAM95 is therefore inhibition of MAN1 (Accession NM_014319). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1. MGC12966 (Accession NM_032706) is another VGAM95 host target gene. MGC12966 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12966, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12966 BINDING SITE, designated SEQ ID:26421, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8878] Another function of VGAM95 is therefore inhibition of MGC12966 (Accession NM_032706). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12966. MGC16063 (Accession NM_053047) is another VGAM95 host target gene. MGC16063 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16063 BINDING SITE, designated SEQ ID:27592, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8879] Another function of VGAM95 is therefore inhibition of MGC16063 (Accession NM_053047). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC16063. Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580) is another VGAM95 host target gene. MKRN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MKRN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN2 BINDING SITE, designated SEQ ID:35858, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8880] Another function of VGAM95 is therefore inhibition of Makorin, Ring Finger Protein, 2 (MKRN2, Accession XM_051580). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN2. Phosphodiesterase 10A (PDE10A, Accession NM_006661) is another VGAM95 host target gene. PDE10A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDE10A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PDE10A BINDING SITE, designated SEQ ID:13462, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8881] Another function of VGAM95 is therefore inhibition of Phosphodiesterase 10A (PDE10A, Accession NM_006661). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE10A. Phosphodiesterase 7B (PDE7B, Accession NM_018945) is another VGAM95 host target gene. PDE7B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PDE7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE7B BINDING SITE, designated SEQ ID:21012, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8882] Another function of VGAM95 is therefore inhibition of Phosphodiesterase 7B (PDE7B, Accession NM_018945). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with PDE7B. Proline Rich 2 (PROL2, Accession NM_006813) is another VGAM95 host target gene. PROL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROL2 BINDING SITE, designated SEQ ID:13685, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8883] Another function of VGAM95 is therefore inhibition of Proline Rich 2 (PROL2, Accession NM_006813). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROL2. SSH2 (Accession XM_030846) is another VGAM95 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31185, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2806.

[8884] Another function of VGAM95 is therefore inhibition of SSH2 (Accession XM_030846). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. LOC122704 (Accession XM_058647) is another VGAM95 host target gene. LOC122704 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122704, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122704 BINDING SITE, designated SEQ ID:36693, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8885] Another function of VGAM95 is therefore inhibition of LOC122704 (Accession XM_058647). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122704. LOC124944 (Accession XM_058876) is another VGAM95 host target gene. LOC124944 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124944, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124944 BINDING SITE, designated SEQ ID:36777, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8886] Another function of VGAM95 is therefore inhibition of LOC124944 (Accession XM_058876). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124944. LOC143153 (Accession XM_084440) is another VGAM95 host target gene. LOC143153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143153 BINDING SITE, designated SEQ ID:37580, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8887] Another function of VGAM95 is therefore inhibition of LOC143153 (Accession XM_084440). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC143153. LOC143154 (Accession XM_084441) is another VGAM95 host target gene. LOC143154 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC143154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143154 BINDING SITE, designated SEQ ID:37587, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8888] Another function of VGAM95 is therefore inhibition of LOC143154 (Accession XM_084441). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143154. LOC144747 (Accession XM_084954) is another VGAM95 host target gene. LOC144747 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144747 BINDING SITE, designated SEQ ID:37784, to

the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8889] Another function of VGAM95 is therefore inhibition of LOC144747 (Accession XM_084954). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144747. LOC146515 (Accession XM_085493) is another VGAM95 host target gene. LOC146515 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146515 BINDING SITE, designated SEQ ID:38194, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8890] Another function of VGAM95 is therefore inhibition of LOC146515 (Accession XM_085493). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146515. LOC147658 (Accession XM_085827) is another VGAM95 host target gene. LOC147658 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC147658, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147658 BINDING SITE, designated SEQ ID:38354, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8891] Another function of VGAM95 is therefore inhibition of LOC147658 (Accession XM_085827). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147658. LOC149175 (Accession XM_086445) is another VGAM95 host target gene. LOC149175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149175 BINDING SITE, designated SEQ ID:38662, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8892] Another function of VGAM95 is therefore inhibition of LOC149175 (Accession XM_086445). Accordingly, utilities

of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149175. LOC151178 (Accession XM_087117) is another VGAM95 host target gene. LOC151178 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151178 BINDING SITE, designated SEQ ID:39072, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8893] Another function of VGAM95 is therefore inhibition of LOC151178 (Accession XM_087117). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151178. LOC158156 (Accession XM_088496) is another VGAM95 host target gene. LOC158156 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC158156 BINDING SITE, designated SEQ ID:39743, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8894] Another function of VGAM95 is therefore inhibition of LOC158156 (Accession XM_088496). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158156. LOC158527 (Accession XM_088594) is another VGAM95 host target gene. LOC158527 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158527 BINDING SITE, designated SEQ ID:39863, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8895] Another function of VGAM95 is therefore inhibition of LOC158527 (Accession XM_088594). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158527. LOC165693 (Accession XM_093373) is another VGAM95 host target gene. LOC165693 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165693 BINDING SITE, designated SEQ ID:40188, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8896] Another function of VGAM95 is therefore inhibition of LOC165693 (Accession XM_093373). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165693. LOC168576 (Accession XM_095191) is another VGAM95 host target gene. LOC168576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC168576, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC168576 BINDING SITE, designated SEQ ID:40255, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8897] Another function of VGAM95 is therefore inhibition of

LOC168576 (Accession XM_095191). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC168576. LOC200301 (Accession XM_114197) is another VGAM95 host target gene. LOC200301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200301 BINDING SITE, designated SEQ ID:42782, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8898] Another function of VGAM95 is therefore inhibition of LOC200301 (Accession XM_114197). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200301. LOC203429 (Accession XM_114701) is another VGAM95 host target gene. LOC203429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC203429 BINDING SITE, designated SEQ ID:43051, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8899] Another function of VGAM95 is therefore inhibition of LOC203429 (Accession XM_114701). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203429. LOC219294 (Accession XM_167566) is another VGAM95 host target gene. LOC219294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219294 BINDING SITE, designated SEQ ID:44688, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8900] Another function of VGAM95 is therefore inhibition of LOC219294 (Accession XM_167566). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219294. LOC219295 (Accession XM_167565) is an-

other VGAM95 host target gene. LOC219295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219295 BINDING SITE, designated SEQ ID:44682, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8901] Another function of VGAM95 is therefore inhibition of LOC219295 (Accession XM_167565). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219295. LOC219401 (Accession XM_166706) is another VGAM95 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44593, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8902] Another function of VGAM95 is therefore inhibition of LOC219401 (Accession XM_166706). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC220705 (Accession XM_166000) is another VGAM95 host target gene. LOC220705 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220705 BINDING SITE, designated SEQ ID:43835, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8903] Another function of VGAM95 is therefore inhibition of LOC220705 (Accession XM_166000). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220705. LOC221540 (Accession XM_168133) is another VGAM95 host target gene. LOC221540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221540, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221540 BINDING SITE, designated SEQ ID:45045, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8904] Another function of VGAM95 is therefore inhibition of LOC221540 (Accession XM_168133). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221540. LOC221833 (Accession XM_166519) is another VGAM95 host target gene. LOC221833 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221833 BINDING SITE, designated SEQ ID:44457, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8905] Another function of VGAM95 is therefore inhibition of LOC221833 (Accession XM_166519). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221833. LOC257354 (Accession XM_170810) is another VGAM95 host target gene. LOC257354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257354 BINDING SITE, designated SEQ ID:45580, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8906] Another function of VGAM95 is therefore inhibition of LOC257354 (Accession XM_170810). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257354. LOC257545 (Accession XM_175217) is another VGAM95 host target gene. LOC257545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257545 BINDING SITE, designated SEQ ID:46693, to the nucleotide sequence of VGAM95 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2806.

[8907] Another function of VGAM95 is therefore inhibition of LOC257545 (Accession XM_175217). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257545. LOC257598 (Accession XM_175295) is another VGAM95 host target gene. LOC257598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257598 BINDING SITE, designated SEQ ID:46750, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8908] Another function of VGAM95 is therefore inhibition of LOC257598 (Accession XM_175295). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257598. LOC51580 (Accession NM_015874) is another VGAM95 host target gene. LOC51580 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51580, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51580 BINDING SITE, designated SEQ ID:18017, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8909] Another function of VGAM95 is therefore inhibition of LOC51580 (Accession NM_015874). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51580. LOC90092 (Accession XM_028862) is another VGAM95 host target gene. LOC90092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90092 BINDING SITE, designated SEQ ID:30791, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8910] Another function of VGAM95 is therefore inhibition of LOC90092 (Accession XM_028862). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC90092. LOC90133 (Accession XM_029323) is another VGAM95 host target gene. LOC90133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90133 BINDING SITE, designated SEQ ID:30870, to the nucleotide sequence of VGAM95 RNA, herein designated VGAM RNA, also designated SEQ ID:2806.

[8911] Another function of VGAM95 is therefore inhibition of LOC90133 (Accession XM_029323). Accordingly, utilities of VGAM95 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90133. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 96 (VGAM96) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8912] VGAM96 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM96 was detected is described hereinabove with reference to Figs. 1–8.

[8913] VGAM96 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8914] VGAM96 gene encodes a VGAM96 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM96 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM96 precursor RNA is designated SEQ ID:82, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:82 is located at position 9897 relative to the genome of Plutella Xylostella Granulovirus.

[8915] VGAM96 precursor RNA folds onto itself, forming VGAM96 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is

due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8916] An enzyme complex designated DICER COMPLEX, `dices` the VGAM96 folded precursor RNA into VGAM96 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM96 RNA is designated SEQ ID:2807, and is provided hereinbelow with reference to the sequence listing part.

[8917] VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM96 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8918] VGAM96 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM96 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM96 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8919] The complementary binding of VGAM96 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM96 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM96 host target RNA into VGAM96 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8920] It is appreciated that VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM96 host target genes. The mRNA of each one of this plurality of VGAM96 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM96 RNA, herein designated VGAM RNA, and which when bound by VGAM96 RNA causes inhibition of translation of respective one or more VGAM96 host target proteins.

[8921] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM96 gene, herein designated VGAM GENE, on one or more VGAM96 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with

reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8922] It is yet further appreciated that a function of VGAM96 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM96 correlate with, and may be deduced from, the identity of the host target genes which VGAM96 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8923] Nucleotide sequences of the VGAM96 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM96 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of

VGAM96 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM96 are further described hereinbelow with reference to Table 1.

[8924] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM96 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM96 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8925] As mentioned hereinabove with reference to Fig. 1, a function of VGAM96 gene, herein designated VGAM is inhibition of expression of VGAM96 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM96 correlate with, and may be deduced from, the identity of the target genes which VGAM96 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8926] Angiotensin II Receptor, Type 1 (AGTR1, Accession NM_031850) is a VGAM96 host target gene. AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGTR1, corresponding to HOST TARGET bind-

ing sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGTR1 BINDING SITE1 through AGTR1 BINDING SITE5, designated SEQ ID:25593, SEQ ID:6341, SEQ ID:11242, SEQ ID:14308 and SEQ ID:25768 respectively, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8927] A function of VGAM96 is therefore inhibition of Angiotensin II Receptor, Type 1 (AGTR1, Accession NM_031850), a gene which is an important effector controlling blood pressure and volume in the cardiovascular system. Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGTR1. The function of AGTR1 has been established by previous studies. Angiotensin II (see OMIM Ref. No. 106150) is an important effector controlling blood pressure and volume in the cardiovascular system. Its importance is reflected by the efficacy of angiotensin-converting enzyme inhibitors in the treatment of hypertension and congestive heart failure. Angiotensin II interacts with 2 pharmacologically distinct subtypes of cell surface receptors, types 1 and 2 (AGTR2; 600350).

Type 1 receptors seem to mediate the major cardiovascular effects of angiotensin II. By expression cloning, Murphy et al. (1991) isolated a cDNA encoding the type 1 receptor. Hydropathic modeling of the deduced protein suggested that it shares the 7-transmembrane-region motif with the G protein-coupled receptor superfamily. Sasaki et al. (1991) isolated the corresponding bovine gene.

Takayanagi et al. (1992) cloned and sequenced a cDNA encoding this receptor in the human, and by Northern blot analysis they demonstrated its expression in human liver, lung, adrenal, and adrenocortical adenomas, but not in pheochromocytomas. Bergsma et al. (1992) and Mauzy et al. (1992) also cloned and characterized a human AGTR1 cDNA. Furuta et al. (1992) studied the genomic sequence and demonstrated that the coding region is contained in a single exon. By comparing genomic DNA and cDNA sequences, Guo et al. (1994) demonstrated that the AGTR1 gene consists of at least 5 exons and spans more than 55 kb of genomic DNA. The size of the exons ranges from 59 to 2,014 bp. Four of the exons encode 5-prime untranslated sequences. Multiple transcription initiation sites were observed by primer extension experiments. Pharmacologic agents that either block the formation of an-

angiotensin II or interrupt its action by antagonizing the AGT1–receptor are highly successful in the treatment of angiotensin II–dependent hypertension. Most notable among these agents is losartan, an AGT1–receptor antagonist that has been found to be an effective anti–hypertension drug without the usual side effects. This, coupled with the demonstration that polymorphism in the AGTR1 gene is associated with hypertension (Bonnardeaux et al., 1994), further supports the notion that the AGT1 receptor is an important target for the control of angiotensin II–dependent hypertension. In spite of the availability of excellent drugs for the control of hypertension, Iyer et al. (1996) explored the possibility that gene therapy could be used. They demonstrated that the delivery of angiotensin type 1 receptor antisense by a retrovirally–mediated delivery system resulted in a selective attenuation of the cellular actions of angiotensin II in the neurons of the spontaneously hypertensive (SH) rat model. A single injection normalized blood pressure in the SH rat on a long–term basis. The use of this approach in patients was proposed. Animal model experiments lend further support to the function of AGTR1. Oliverio et al. (1998) generated mice lacking AT1B (*Agtr1b* –/–) and other mice lacking

both AT1A and AT1B receptors. Agtr1b $-/-$ mice were healthy, without an abnormal phenotype. In contrast, mice who were homozygous for disruptions of both Agtr1a and Agtr1b had diminished growth, vascular thickening within the kidney, and atrophy of the inner renal medulla. This phenotype was virtually identical to that seen in angiotensinogen-deficient mice (see OMIM Ref. No. 106150) and in mice deficient in angiotensin-converting enzyme (OMIM Ref. No. 106180). The double knockout mice had no systemic pressor response to infusions of angiotensin II, but they responded normally to another vasoconstrictor, epinephrine. Blood pressure was reduced substantially in the double knockout mice, and following administration of an angiotensin-converting enzyme inhibitor, their blood pressure increased paradoxically.

[8928] It is appreciated that the abovementioned animal model for AGTR1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[8929] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8930] Oliverio, M. I.; Kim, H-S.; Ito, M.; Le, T.; Audoly, L.; Best,

C. F.; Hiller, S.; Kluckman, K.; Maeda, N.; Smithies, O.; Coffman, T. M. : Reduced growth, abnormal kidney structure, and type 2 (AT2) angiotensin receptor-mediated blood pressure regulation in mice lacking both AT1A and AT1B receptors for angiotensin II. Proc. Nat. Acad. Sci. 95: 15496–15501, 1998. ; and

[8931] Iyer, S. N.; Lu, D.; Katovich, M. J.; Raizada, M. K. : Chronic control of high blood pressure in the spontaneously hypertensive rat by delivery of angiotensin type 1 receptor antisense.

[8932] Further studies establishing the function and utilities of AGTR1 are found in John Hopkins OMIM database record ID 106165, and in cited publications numbered 4238–4255, 4258–4257, 4259–426 and 4315–4317 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ10853 (Accession NM_018246) is another VGAM96 host target gene. FLJ10853 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated

SEQ ID:20210, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8933] Another function of VGAM96 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. KIAA0189 (Accession NM_014725) is another VGAM96 host target gene. KIAA0189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0189 BINDING SITE, designated SEQ ID:16316, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8934] Another function of VGAM96 is therefore inhibition of KIAA0189 (Accession NM_014725). Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0189. KIAA1100 (Accession NM_014901) is another VGAM96 host target gene. KIAA1100 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1100 BINDING SITE, designated SEQ ID:17085, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8935] Another function of VGAM96 is therefore inhibition of KIAA1100 (Accession NM_014901). Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1100. Phosphodiesterase 8A (PDE8A, Accession XM_031443) is another VGAM96 host target gene. PDE8A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE8A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE8A BINDING SITE, designated SEQ ID:31378, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8936] Another function of VGAM96 is therefore inhibition of

Phosphodiesterase 8A (PDE8A, Accession XM_031443). Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE8A. LOC149832 (Accession XM_097733) is another VGAM96 host target gene.

LOC149832 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149832 BINDING SITE, designated SEQ ID:41077, to the nucleotide sequence of VGAM96 RNA, herein designated VGAM RNA, also designated SEQ ID:2807.

[8937] Another function of VGAM96 is therefore inhibition of LOC149832 (Accession XM_097733). Accordingly, utilities of VGAM96 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149832. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 97 (VGAM97) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[8938] VGAM97 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM97 was detected is described hereinabove with reference to Figs. 1–8.

[8939] VGAM97 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8940] VGAM97 gene encodes a VGAM97 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM97 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM97 precursor RNA is designated SEQ ID:83, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:83 is located at position 1601 relative to the genome of Plutella Xylostella Granulovirus.

[8941] VGAM97 precursor RNA folds onto itself, forming VGAM97 folded precursor RNA, herein designated VGAM FOLDED

PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8942] An enzyme complex designated DICER COMPLEX, `dices` the VGAM97 folded precursor RNA into VGAM97 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM97 RNA is designated SEQ ID:2808, and is provided hereinbelow with reference to the sequence listing part.

[8943] VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM97 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a

5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8944] VGAM97 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM97 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM97 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR

region, or in both 3`UTR and 5`UTR regions.

[8945] The complementary binding of VGAM97 RNA, herein designated VGAM RNA, to host target binding sites on VGAM97 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM97 host target RNA into VGAM97 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8946] It is appreciated that VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM97 host target genes. The mRNA of each one of this plurality of VGAM97 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM97 RNA, herein designated VGAM RNA, and which when bound by VGAM97 RNA causes inhibition of translation of respective one or more VGAM97 host target proteins.

[8947] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM97 gene, herein designated VGAM GENE, on one or

more VGAM97 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8948] It is yet further appreciated that a function of VGAM97 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM97 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM97 correlate with, and may be deduced from, the identity of the host target genes which VGAM97 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8949] Nucleotide sequences of the VGAM97 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM97 RNA, herein designated VGAM RNA, and
a schematic representation of the secondary folding of
VGAM97 folded precursor RNA, herein designated VGAM
FOLDED PRECURSOR RNA, of VGAM97 are further de-
scribed hereinbelow with reference to Table 1.

[8950] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM97 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM97 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[8951] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM97 gene, herein designated VGAM is in-
hibition of expression of VGAM97 target genes. It is ap-
preciated that specific functions, and accordingly utilities,
of VGAM97 correlate with, and may be deduced from, the
identity of the target genes which VGAM97 binds and in-
hibits, and the function of these target genes, as elabo-
rated hereinbelow.

[8952] FLJ11618 (Accession NM_022452) is a VGAM97 host tar-
get gene. FLJ11618 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by FLJ11618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11618 BINDING SITE, designated SEQ ID:22793, to the nucleotide sequence of VGAM97 RNA, herein designated VGAM RNA, also designated SEQ ID:2808.

[8953] A function of VGAM97 is therefore inhibition of FLJ11618 (Accession NM_022452). Accordingly, utilities of VGAM97 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11618. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 98 (VGAM98) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8954] VGAM98 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM98 was detected is described hereinabove with reference to Figs. 1–8.

[8955] VGAM98 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Plutella Xylostella Granulovirus. VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8956] VGAM98 gene encodes a VGAM98 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM98 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM98 precursor RNA is designated SEQ ID:84, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:84 is located at position 52717 relative to the genome of Plutella Xylostella Granulovirus.

[8957] VGAM98 precursor RNA folds onto itself, forming VGAM98 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8958] An enzyme complex designated DICER COMPLEX, `dices` the VGAM98 folded precursor RNA into VGAM98 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM98 RNA is designated SEQ ID:2809, and is provided hereinbelow with reference to the sequence listing part.

[8959] VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM98 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[8960] VGAM98 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. This com-

plementary binding is due to the fact that the nucleotide sequence of VGAM98 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM98 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[8961] The complementary binding of VGAM98 RNA, herein designated VGAM RNA, to host target binding sites on VGAM98 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM98 host target RNA into VGAM98 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8962] It is appreciated that VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM98 host target genes. The mRNA of each one of this plurality of VGAM98 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM98 RNA, herein designated VGAM RNA, and which when bound by VGAM98 RNA causes inhibition of translation of respective one or more VGAM98 host target proteins.

[8963] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM98 gene, herein designated VGAM GENE, on one or more VGAM98 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also

believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8964] It is yet further appreciated that a function of VGAM98 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM98 correlate with, and may be deduced from, the identity of the host target genes which VGAM98 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8965] Nucleotide sequences of the VGAM98 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM98 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM98 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM98 are further described hereinbelow with reference to Table 1.

[8966] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM98 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM98 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8967] As mentioned hereinabove with reference to Fig. 1, a function of VGAM98 gene, herein designated VGAM is inhibition of expression of VGAM98 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM98 correlate with, and may be deduced from, the identity of the target genes which VGAM98 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8968] Core-binding Factor, Beta Subunit (CBFB, Accession NM_001755) is a VGAM98 host target gene. CBFB BINDING SITE1 and CBFB BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBFB, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFB BINDING SITE1 and CBFB BINDING SITE2, designated SEQ ID:7505 and SEQ ID:23146 respectively, to

the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8969] A function of VGAM98 is therefore inhibition of Core-binding Factor, Beta Subunit (CBFB, Accession NM_001755), a gene which is beta subunit of the transcription factor CBF which causes leukemia. Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFB. The function of CBFB has been established by previous studies. Liu et al. (1995) provided a review of leukemia pathogenesis related to CBFB. They suggested that it will be interesting to see whether variant fusions between CBFB and another gene exist as a result of translocation between 16q and another chromosome. The study of such variants might shed light on the mechanism of genesis by the inversion 16 fusion gene. Whether the abnormal eosinophils in the circulation in patients with inv(16) are part of the malignant cell population or a result of a secondary response could not be determined. Although the distribution of breakpoints in the introns of the 2 participating genes was heterogeneous, a surprisingly high incidence of breaks was observed in a small (OMIM Ref. No. 370 bp) intron of the MYH11 gene. CBFB

and AML1 encode the 2 subunits of the transcription factor CBF, and alterations of either one are associated with acute myeloid leukemia. CBFB is a transcription factor that does not bind DNA directly but interacts with the AML1 DNA-binding transcription factor (AML1) to increase its ability to bind DNA and regulate transcription. AML1 is one of the most frequently mutated genes in human leukemia. It is disrupted by the t(8;21), t(3;21), and t(16;21) in acute myeloid leukemia and by the t(12;21) in childhood B-cell acute lymphocytic leukemia (ALL). By disrupting CBFB, the inv(16) also disrupts AML1 functions. Together, these chromosomal rearrangements account for nearly one-quarter of all AML cases and one-fifth of all childhood B cell ALL-containing discernible chromosomal abnormalities. Lutterbach et al. (1999) showed that the inv(16) fusion protein cooperates with the largest form of AML1, termed AML-1B, to repress transcription. This cooperativity requires the ability of the translocation fusion protein to bind to AML-1B. Mutation analysis and cell fractionation experiments indicated that the inv(16) fusion protein acts in the nucleus and that repression occurs when the complex is bound to DNA. They demonstrated that the C-terminal portion of the inv(16) fusion protein

contains a repression domain, suggesting a molecular mechanism for AML1-mediated repression.

[8970] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[8971] Liu, P.; Tarle, S. A.; Hajra, A.; Claxton, D. F.; Marlton, P.; Freedman, M.; Siciliano, M. J.; Collins, F. S. : Fusion between transcription factor CBF-beta/PEBP2-beta and a myosin heavy chain in acute myeloid leukemia. Science 261: 1041-1044, 1993. ; and

[8972] Lutterbach, B.; Hou, Y.; Durst, K. L.; Hiebert, S. W. : The inv(16) encodes an acute myeloid leukemia 1 transcriptional corepressor. Proc. Nat. Acad. Sci. 96: 12822-12827, 1999.

[8973] Further studies establishing the function and utilities of CBFB are found in John Hopkins OMIM database record ID 121360, and in cited publications numbered 3402-3408 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sorting Nexin 9 (SNX9, Accession NM_016224) is another VGAM98 host target gene. SNX9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX9, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX9 BINDING SITE, designated SEQ ID:18329, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8974] Another function of VGAM98 is therefore inhibition of Sorting Nexin 9 (SNX9, Accession NM_016224). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX9. T-complex-associated-testis-expressed 1-like (TCTE1L, Accession XM_048205) is another VGAM98 host target gene. TCTE1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCTE1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCTE1L BINDING SITE, designated SEQ ID:35142, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8975] Another function of VGAM98 is therefore inhibition of T-complex-associated-testis-expressed 1-like (TCTE1L, Ac-

cession XM_048205). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCTE1L. Translin (TSN, Accession NM_004622) is another VGAM98 host target gene. TSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSN BINDING SITE, designated SEQ ID:10984, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8976] Another function of VGAM98 is therefore inhibition of Translin (TSN, Accession NM_004622), a gene which is a DNA binding protein and involved in DNA repair, replication, or recombination. Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSN. The function of TSN has been established by previous studies. Kasai et al. (1994) identified a protein they termed recombination hotspot-associated factor (RCHF1), which specifically binds to the signal-like sequences at the breakpoint junction of 8q24 and 1p32 in acute lymphoblastic leukemia

(ALL) patients carrying t(8;14)(q24;q11) and t(1;14)(p32;q11) translocations involving the TCR delta-chain locus (TCRD; 186810). Aoki et al. (1994) showed that an analogous protein, which they designated BCLF1, specifically binds to a target sequence within the clustered breakpoint region of the BCL2 oncogene (OMIM Ref. No. 151430) in follicular lymphoma patients carrying t(14;18)(q32;q21) translocations. It was proposed that these binding activities at recombination hotspot regions may play a crucial role in chromosomal translocations in lymphoid neoplasms. Aoki et al. (1995) purified the BCLF1 protein to homogeneity and determined that it is identical to RCHF1. Molecular gene cloning experiments revealed that the purified protein, which they named translin (TSN), is a previously undescribed DNA-binding protein with no significant similarity to known proteins. (The designation 'translin' came from selected letters in 'translocation.')

In addition, Aoki et al. (1995) found that nuclear localization of translin was limited to lymphoid cell lines with rearranged Ig and processes such as DNA repair, replication, or recombination. In their native form, translin polypeptides form a multimeric structure that is responsible for its DNA binding activity. Aoki et al. (1997) found that the

human and mouse translin genes have identical genomic structures consisting of 6 exons, 5 introns, and a GC-rich upstream region. By in situ hybridization and analysis of somatic cell hybrids, Aoki et al. (1997) mapped the human TSN gene to 2q21.1. Badge et al. (2000) studied a sub-telomeric region at 16p13.3 that displays a 300-fold increase in crossovers compared to the genomic average rate. Segregation analysis of CEPH and other pedigrees yielded 6 paternal crossover breakpoints in the approximately 85-kb interval between the minisatellite loci D16S309 (MS205) and D16S83 (OMIM Ref. No. EKMDA2). Three crossovers were mapped to within the same small (less than 3 kb) interval, which did not colocalize with any tandem repeat array or expressed sequence. Sequence analysis revealed the presence of recombination-associated motifs and binding sites for translin. The authors concluded that this locus represents an intense male-specific recombination hotspot. Hosaka et al. (2000) demonstrated that the presence of the translin binding motif may be one of the important determinants for the location of breakpoints in the TLS (OMIM Ref. No. 137070) and CHOP (OMIM Ref. No. 126337) genes which are fused by translocation t(12;16) in liposarcomas.

- [8977] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [8978] Badge, R. M.; Yardley, J.; Jeffreys, A. J.; Armour, J. A. L. : Crossover breakpoint mapping identifies a subtelomeric hotspot for male meiotic recombination. *Hum. Molec. Genet.* 9: 1239–1244, 2000. ; and
- [8979] Hosaka, T.; Kanoe, H.; Nakayama, T.; Murakami, H.; Yamamoto, H.; Nakamata, T.; Tsuboyama, T.; Oka, M.; Kasai, M.; Sasaki, M. S.; Nakamura, T.; Toguchida, J. : Translin binds to the sequ.
- [8980] Further studies establishing the function and utilities of TSN are found in John Hopkins OMIM database record ID 600575, and in cited publications numbered 9536–953 and 9914–9917 listed in the bibliography section herein–below, which are also hereby incorporated by reference. NTT73 (Accession NM_018057) is another VGAM98 host target gene. NTT73 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NTT73, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTT73 BINDING SITE, des–

ignated SEQ ID:19823, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8981] Another function of VGAM98 is therefore inhibition of NTT73 (Accession NM_018057). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTT73. Nudix (nucleoside diphosphate linked moiety X)-type Motif 11 (NUDT11, Accession XM_010230) is another VGAM98 host target gene. NUDT11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUDT11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUDT11 BINDING SITE, designated SEQ ID:30145, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8982] Another function of VGAM98 is therefore inhibition of Nudix (nucleoside diphosphate linked moiety X)-type Motif 11 (NUDT11, Accession XM_010230). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

NUDT11. POPX1 (Accession NM_014906) is another VGAM98 host target gene. POPX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by POPX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POPX1 BINDING SITE, designated SEQ ID:17118, to the nucleotide sequence of VGAM98 RNA, herein designated VGAM RNA, also designated SEQ ID:2809.

[8983] Another function of VGAM98 is therefore inhibition of POPX1 (Accession NM_014906). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POPX1. Tripartite Motif-containing 2 (TRIM2, Accession NM_015271) is another VGAM98 host target gene. TRIM2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM2 BINDING SITE, designated SEQ ID:17598, to the nucleotide sequence of VGAM98 RNA, herein designated

VGAM RNA, also designated SEQ ID:2809.

[8984] Another function of VGAM98 is therefore inhibition of Tripartite Motif-containing 2 (TRIM2, Accession NM_015271). Accordingly, utilities of VGAM98 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 99 (VGAM99) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[8985] VGAM99 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM99 was detected is described hereinabove with reference to Figs. 1–8.

[8986] VGAM99 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[8987] VGAM99 gene encodes a VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM99 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM99 precursor RNA is designated SEQ ID:85, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:85 is located at position 37560 relative to the genome of *Plutella Xylostella Granulovirus*.

[8988] VGAM99 precursor RNA folds onto itself, forming VGAM99 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[8989] An enzyme complex designated DICER COMPLEX, `dices` the VGAM99 folded precursor RNA into VGAM99 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM99 RNA is designated SEQ ID:2810, and is provided hereinbelow with reference to the sequence listing part.

[8990] VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM99 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[8991] VGAM99 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM99 RNA is an accurate or a partial inverted-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III

respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM99 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[8992] The complementary binding of VGAM99 RNA, herein designated VGAM RNA, to host target binding sites on VGAM99 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM99 host target RNA into VGAM99 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[8993] It is appreciated that VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM99 host target genes. The mRNA of each one of this plurality of VGAM99 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM99 RNA, herein designated VGAM RNA, and which when bound by VGAM99 RNA causes inhibition of translation of respective one or more VGAM99 host target proteins.

[8994] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM99 gene, herein designated VGAM GENE, on one or more VGAM99 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[8995] It is yet further appreciated that a function of VGAM99 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM99 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM99 correlate with, and may be deduced from, the identity of the host target genes which VGAM99 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[8996] Nucleotide sequences of the VGAM99 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM99 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM99 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM99 are further described hereinbelow with reference to Table 1.

[8997] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM99 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM99 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[8998] As mentioned hereinabove with reference to Fig. 1, a function of VGAM99 gene, herein designated VGAM is inhibition of expression of VGAM99 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM99 correlate with, and may be deduced from, the identity of the target genes which VGAM99 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[8999] Translin (TSN, Accession NM_004622) is a VGAM99 host target gene. TSN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSN BINDING SITE, designated SEQ ID:10985, to the nucleotide sequence of VGAM99 RNA, herein designated VGAM RNA, also designated SEQ ID:2810.

[9000] A function of VGAM99 is therefore inhibition of Translin (TSN, Accession NM_004622), a gene which is a DNA binding protein and involved in DNA repair, replication, or recombination. Accordingly, utilities of VGAM99 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with TSN. The function of TSN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM98.KIAA1535 (Accession XM_086565) is another VGAM99 host target gene. KIAA1535 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1535 BINDING SITE, designated SEQ ID:38764, to the nucleotide sequence of VGAM99 RNA, herein designated VGAM RNA, also designated SEQ ID:2810.

[9001] Another function of VGAM99 is therefore inhibition of KIAA1535 (Accession XM_086565). Accordingly, utilities of VGAM99 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1535. NECL1 (Accession NM_021189) is another VGAM99 host target gene. NECL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NECL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NECL1 BINDING SITE, designated SEQ ID:22163, to the nucleotide sequence of VGAM99 RNA, herein designated VGAM RNA, also designated SEQ ID:2810.

[9002] Another function of VGAM99 is therefore inhibition of NECL1 (Accession NM_021189). Accordingly, utilities of VGAM99 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NECL1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 100 (VGAM100) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9003] VGAM100 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM100 was detected is described hereinabove with reference to Figs. 1–8.

[9004] VGAM100 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in

the human genome.

[9005] VGAM100 gene encodes a VGAM100 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM100 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM100 precursor RNA is designated SEQ ID:86, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:86 is located at position 61363 relative to the genome of *Plutella Xylostella Granulovirus*.

[9006] VGAM100 precursor RNA folds onto itself, forming VGAM100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9007] An enzyme complex designated DICER COMPLEX, `dices` the VGAM100 folded precursor RNA into VGAM100 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM100 RNA is designated SEQ ID:2811, and is provided hereinbelow with reference to the sequence listing part.

[9008] VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM100 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9009] VGAM100 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM100 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM100 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9010] The complementary binding of VGAM100 RNA, herein designated VGAM RNA, to host target binding sites on VGAM100 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM100 host target RNA into VGAM100 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9011] It is appreciated that VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM100 host target genes. The mRNA of each one of this plurality of VGAM100 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM100 RNA, herein designated VGAM RNA, and which when bound by VGAM100 RNA causes inhibition of translation of respective one or more VGAM100 host target proteins.

[9012] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM100 gene, herein designated VGAM GENE, on one or more VGAM100 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9013] It is yet further appreciated that a function of VGAM100 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM100 correlate with, and may be deduced from, the identity of the host target genes which VGAM100 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9014] Nucleotide sequences of the VGAM100 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM100 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM100 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM100 are further described hereinbelow with reference to Table 1.

[9015] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM100 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM100 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9016] As mentioned hereinabove with reference to Fig. 1, a function of VGAM100 gene, herein designated VGAM is inhibition of expression of VGAM100 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM100 correlate with, and may be deduced from, the identity of the target genes which VGAM100 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9017] Nuclear Factor I/B (NFIB, Accession NM_005596) is a VGAM100 host target gene. NFIB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFIB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFIB BINDING SITE, designated SEQ ID:12120, to the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA, also designated SEQ ID:2811.

[9018] A function of VGAM100 is therefore inhibition of Nuclear Factor I/B (NFIB, Accession NM_005596), a gene which recognizes and binds the palindromic sequence 5'- ttggc-nnnnngccaa-3' present in viral and cellular promoters. Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFIB. The function of NFIB has been established by previous studies. See nuclear factor I/A (NFIA; 600727). Qian et al. (1995) mapped the NFIB gene to chromosome 9p24.1 by fluorescence in situ hybridization. Approximately 12% of all pleomorphic adenomas of the salivary glands are characterized by chromosome aberrations involving 12q13-q15. Several chromosomes have been found as translocation partners of chromosome 12, and some of these are recurrent. The target gene on 12q13-q15 involved in the translocation is HMGIC (OMIM Ref. No. 600698). Fusion partner genes include LPP (OMIM Ref. No. 600700) on 3q, ALDH2 (OMIM Ref. No. 100650) on 12q24.1, and FHIT (OMIM Ref. No. 601153) on 3p. Using 3-prime-RACE analysis of a primary adenoma with an apparently normal karyotype, Geurts et al. (1998) found an HMGIC fusion transcript containing ectopic sequences derived from the NFIB gene. In a second adenoma with an

ins(9;12)(p23;q12q15) as the sole anomaly, they also found an HMGIC/NFIB hybrid transcript. Nucleotide sequence analysis of the fusion transcripts indicated that the genetic aberration in both tumors resulted in the replacement of a carboxy-terminal segment of HMGIC by the last 5 amino acids of NFIB

[9019] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9020] Geurts, J. M. W.; Schoenmakers, E. F. P. M.; Roijer, E.; Astrom, A.-K.; Stenman, G.; van de Ven, W. J. M. : Identification of NFIB as recurrent translocation partner gene of HMGIC in pleomorphic adenomas. *Oncogene* 16: 865-872, 1998. ; and

[9021] Qian, F.; Kruse, U.; Lichter, P.; Sippel, A. E. : Chromosomal localization of the four genes (NFIA, B, C, and X) for the human transcription factor nuclear factor I by FISH. *Genomics* 28.

[9022] Further studies establishing the function and utilities of NFIB are found in John Hopkins OMIM database record ID 600728, and in cited publications numbered 7133 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp434J0617

(Accession NM_032246) is another VGAM100 host target gene. DKFZp434J0617 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434J0617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434J0617 BINDING SITE, designated SEQ ID:25980, to the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA, also designated SEQ ID:2811.

[9023] Another function of VGAM100 is therefore inhibition of DKFZp434J0617 (Accession NM_032246). Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434J0617. LCE (Accession NM_024090) is another VGAM100 host target gene. LCE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LCE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LCE BINDING SITE, designated SEQ ID:23532, to the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA,

also designated SEQ ID:2811.

[9024] Another function of VGAM100 is therefore inhibition of LCE (Accession NM_024090). Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LCE. mPA-PLA1 (Accession NM_139248) is another VGAM100 host target gene. mPA-PLA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by mPA-PLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of mPA-PLA1 BINDING SITE, designated SEQ ID:29249, to the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA, also designated SEQ ID:2811.

[9025] Another function of VGAM100 is therefore inhibition of mPA-PLA1 (Accession NM_139248). Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with mPA-PLA1. LOC158629 (Accession XM_098972) is another VGAM100 host target gene. LOC158629 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158629, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158629 BINDING SITE, designated SEQ ID:42018, to the nucleotide sequence of VGAM100 RNA, herein designated VGAM RNA, also designated SEQ ID:2811.

[9026] Another function of VGAM100 is therefore inhibition of LOC158629 (Accession XM_098972). Accordingly, utilities of VGAM100 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158629. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 101 (VGAM101) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9027] VGAM101 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM101 was detected is described hereinabove with reference to Figs. 1–8.

[9028] VGAM101 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Plutella Xylostella* Gran-

ulovirus. VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9029] VGAM101 gene encodes a VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM101 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM101 precursor RNA is designated SEQ ID:87, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:87 is located at position 22037 relative to the genome of Plutella Xylostella Granulovirus.

[9030] VGAM101 precursor RNA folds onto itself, forming VGAM101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9031] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM101 folded precursor RNA into VGAM101 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM101 RNA is designated SEQ ID:2812, and is provided hereinbelow with reference to the sequence listing part.

[9032] VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM101 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9033] VGAM101 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM101 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM101 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9034] The complementary binding of VGAM101 RNA, herein designated VGAM RNA, to host target binding sites on VGAM101 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM101 host target RNA into VGAM101 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9035] It is appreciated that VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM101 host target genes. The mRNA of each one of this plurality of VGAM101 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM101 RNA, herein designated VGAM RNA, and which when bound by VGAM101 RNA causes inhibition of translation of respective one or more VGAM101 host target proteins.

[9036] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM101 gene, herein designated VGAM GENE, on one or more VGAM101 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9037] It is yet further appreciated that a function of VGAM101 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM101 correlate with, and may be deduced from, the identity of the host target genes which VGAM101 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9038] Nucleotide sequences of the VGAM101 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM101 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM101 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM101 are further described hereinbelow with reference to Table 1.

[9039] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM101 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM101 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9040] As mentioned hereinabove with reference to Fig. 1, a function of VGAM101 gene, herein designated VGAM is inhibition of expression of VGAM101 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM101 correlate with, and may be deduced from, the identity of the target genes which VGAM101 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9041] Ferrochelatase (protoporphyrin) (FECH, Accession NM_000140) is a VGAM101 host target gene. FECH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FECH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FECH BINDING SITE, designated SEQ ID:5636, to the nucleotide

sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9042] A function of VGAM101 is therefore inhibition of Ferrochelatase (protoporphyrinogen oxidase) (FECH, Accession NM_000140). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FECH. Heparan Sulfate (glucosamine) 3-O-sulfotransferase 2 (HS3ST2, Accession NM_006043) is another VGAM101 host target gene. HS3ST2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HS3ST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS3ST2 BINDING SITE, designated SEQ ID:12680, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9043] Another function of VGAM101 is therefore inhibition of Heparan Sulfate (glucosamine) 3-O-sulfotransferase 2 (HS3ST2, Accession NM_006043), a gene which plays a role in the generation of heparan sulfate proteoglycan. Accordingly, utilities of VGAM101 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with HS3ST2. The function of HS3ST2 has been established by previous studies. By searching an EST database for sequences related to the sulfotransferase domain of 3OST1, Shworak et al. (1999) identified partial cDNAs from the 3OST2, 3OST3A1 (OMIM Ref. No. 604057), and 3OST4 (OMIM Ref. No. 604059) genes. They used the partial cDNAs as probes and recovered additional clones corresponding to these genes and to 3OST3B1 (OMIM Ref. No. 604058). The 3OST2 gene encodes a predicted 367-amino acid protein that, like 3OST3A1 and 3OST3B1, is a predicted type II integral membrane protein. These 3 enzymes contain a positively charged N-terminal domain, a transmembrane domain, a region termed the SPLAG domain because it is rich in serine, proline, leucine, alanine, and glycine, and a C-terminal putative sulfotransferase domain. Although they share a similar regional structure, the only significant sequence homology between these 3OST proteins occurs in the sulfotransferase domains. Northern blot analysis revealed that the 3OST2 and 3OST4 genes were expressed predominantly in brain, while the 3OST3 gene exhibited more widespread expression. In a companion paper, Liu et al.

(1999) demonstrated that the 3OST1, 3OST2, and 3OST3 isoforms each generate unique 3-O-sulfated structures. Shworak et al. (1999) stated that the isoforms with different sulfotransferase domains differentially place the rare 3-O-sulfate group in distinct sequence contexts, presumably to regulate discrete biologic activities. This capacity of the sulfotransferase domain to generate distinct sequences may in turn be modulated by the unique N-terminal domains of the proteins. By inclusion within mapped clones, Shworak et al. (1999) mapped the 3OST2 gene to 16p12, near the 3OST4 gene at 16p11.2. Using interspecific backcross analysis, they mapped the mouse 3Ost2 and 3Ost4 genes to the distal region of chromosome 7, in a region sharing homology of synteny with human chromosome 16p.

[9044] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9045] Liu, J.; Shworak, N. W.; Sinay, P.; Schwartz, J. J.; Zhang, L.; Fritze, L. M.; Rosenberg, R. D. : Expression of heparan sulfate D-glucosaminyl 3-O-sulfotransferase isoforms reveals novel substrate specificities. J. Biol. Chem. 274: 5185-5192, 1999. ; and

[9046] Shworak, N. W.; Liu, J.; Petros, L. M.; Zhang, L.; Kobayashi, M.; Copeland, N. G.; Jenkins, N. A.; Rosenberg, R. D. : Multiple isoforms of heparan sulfate D-glucosaminyl 3-O-sulfotransf.

[9047] Further studies establishing the function and utilities of HS3ST2 are found in John Hopkins OMIM database record ID 604056, and in cited publications numbered 5054–5055 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 5'-nucleotidase, Cytosolic II (NT5C2, Accession NM_012229) is another VGAM101 host target gene. NT5C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NT5C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NT5C2 BINDING SITE, designated SEQ ID:14524, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9048] Another function of VGAM101 is therefore inhibition of 5'-nucleotidase, Cytosolic II (NT5C2, Accession NM_012229). Accordingly, utilities of VGAM101 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NT5C2. Nuclear RNA Export Factor 5 (NXF5, Accession NM_033153) is another VGAM101 host target gene. NXF5 BINDING SITE1 and NXF5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NXF5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXF5 BINDING SITE1 and NXF5 BINDING SITE2, designated SEQ ID:27006 and SEQ ID:27007 respectively, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9049] Another function of VGAM101 is therefore inhibition of Nuclear RNA Export Factor 5 (NXF5, Accession NM_033153). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXF5. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_002713) is another VGAM101 host target gene. PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R8, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3, designated SEQ ID:8570, SEQ ID:15340 and SEQ ID:28856 respectively, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9050] Another function of VGAM101 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_002713), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 has been established by previous studies. In *Escherichia coli*, the *rne* gene encodes RNase E, a protein involved in RNA degradation. Wang and Cohen (1994) cloned a human gene, which they called ARD1 for 'activator of RNA decay,' that is able to complement mutations in the *E. coli rne* gene. The human ARD1 gene encodes a proline-rich 127-amino acid protein with a predicted mass of 13.3 kD. Wang and Cohen (1994) showed that human ARD1 protein is able to produce RNase E-specific

cleavages in *E. coli*. Van Eynde et al. (1995) cloned the bovine NIPP1 gene. The 351-amino acid NIPP1 protein is a specific inhibitor of type 1 serine/threonine protein phosphatases. The human ARD1 amino acid sequence is virtually identical to the carboxy terminus of the bovine NIPP1 amino acid sequence. Because the homology also extends into noncoding regions, the authors asserted that the NIPP1 and ARD1 proteins are alternately spliced products of the same gene. Claverie-Martin et al. (1997) purified human ARD1 protein and found that its apparent size was 19 kD. They attributed the observed retarded mobility on SDS-PAGE to the highly charged residues at the ends of the protein. Enzyme assays showed that ARD1, like RNase E, is Mg^{2+} dependent and that ARD1 and RNase E cleave RNA at the same sites in A+U-rich regions. Wang (1995) showed that the common 3-prime untranslated region of ARD1 and NIPP1 maps to human chromosome

[9051] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9052] Claverie-Martin, F.; Wang, M.; Cohen, S. N. : ARD-1 cDNA from human cells encodes a site-specific single-strand endoribonuclease that functionally resembles *Escherichia*

coli RNase E. J. Biol. Chem. 272: 13823–13828, 1997. ;
and

[9053] Van Eynde, A.; Wera, S.; Beullens, M.; Torrekens, S.; Van Leuven, F.; Stalmans, W.; Bollen, M. : Molecular cloning of NIPP–1, a nuclear inhibitor of protein phosphatase–1, reveals homolo.

[9054] Further studies establishing the function and utilities of PPP1R8 are found in John Hopkins OMIM database record ID 602636, and in cited publications numbered 8753–875 and 8941–8942 listed in the bibliography section herein–below, which are also hereby incorporated by reference.FLJ10178 (Accession NM_018015) is another VGAM101 host target gene. FLJ10178 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10178 BINDING SITE, designated SEQ ID:19754, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9055] Another function of VGAM101 is therefore inhibition of FLJ10178 (Accession NM_018015). Accordingly, utilities of

VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10178. Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571) is another VGAM101 host target gene. HEYL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEYL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEYL BINDING SITE, designated SEQ ID:15932, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9056] Another function of VGAM101 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEYL. KIAA0173 (Accession NM_014640) is another VGAM101 host target gene. KIAA0173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0173 BINDING SITE, designated SEQ ID:16042, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9057] Another function of VGAM101 is therefore inhibition of KIAA0173 (Accession NM_014640). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0173. Nucleosomal Binding Protein 1 (NSBP1, Accession NM_030763) is another VGAM101 host target gene. NSBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NSBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NSBP1 BINDING SITE, designated SEQ ID:25045, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9058] Another function of VGAM101 is therefore inhibition of Nucleosomal Binding Protein 1 (NSBP1, Accession NM_030763). Accordingly, utilities of VGAM101 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with NSBP1. PRO1257 (Accession NM_018578) is another VGAM101 host target gene.

PRO1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1257 BINDING SITE, designated SEQ ID:20657, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9059] Another function of VGAM101 is therefore inhibition of PRO1257 (Accession NM_018578). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1257. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM101 host target gene. ZDHHC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of ZDHHC2 BINDING SITE, designated SEQ ID:18492, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9060] Another function of VGAM101 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC118851 (Accession XM_061180) is another VGAM101 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, designated SEQ ID:37204, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9061] Another function of VGAM101 is therefore inhibition of LOC118851 (Accession XM_061180). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC118851. LOC145813 (Accession XM_096873) is another VGAM101 host target gene. LOC145813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145813 BINDING SITE, designated SEQ ID:40597, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9062] Another function of VGAM101 is therefore inhibition of LOC145813 (Accession XM_096873). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145813. LOC220565 (Accession XM_165417) is another VGAM101 host target gene. LOC220565 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220565 BINDING SITE, designated SEQ ID:43630, to the nucleotide sequence of VGAM101 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2812.

[9063] Another function of VGAM101 is therefore inhibition of LOC220565 (Accession XM_165417). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220565. LOC85414 (Accession NM_033102) is another VGAM101 host target gene. LOC85414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC85414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC85414 BINDING SITE, designated SEQ ID:26953, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9064] Another function of VGAM101 is therefore inhibition of LOC85414 (Accession NM_033102). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85414. LOC90141 (Accession XM_029373) is another VGAM101 host target gene. LOC90141 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90141, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90141 BINDING SITE, designated SEQ ID:30882, to the nucleotide sequence of VGAM101 RNA, herein designated VGAM RNA, also designated SEQ ID:2812.

[9065] Another function of VGAM101 is therefore inhibition of LOC90141 (Accession XM_029373). Accordingly, utilities of VGAM101 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90141. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 102 (VGAM102) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9066] VGAM102 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM102 was detected is described hereinabove with reference to Figs. 1–8.

[9067] VGAM102 gene, herein designated VGAM GENE, is a viral gene contained in the genome of *Plutella Xylostella* Gran-

ulovirus. VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9068] VGAM102 gene encodes a VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM102 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM102 precursor RNA is designated SEQ ID:88, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:88 is located at position 99184 relative to the genome of Plutella Xylostella Granulovirus.

[9069] VGAM102 precursor RNA folds onto itself, forming VGAM102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9070] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM102 folded precursor RNA into VGAM102 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM102 RNA is designated SEQ ID:2813, and is provided hereinbelow with reference to the sequence listing part.

[9071] VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM102 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9072] VGAM102 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM102 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM102 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9073] The complementary binding of VGAM102 RNA, herein designated VGAM RNA, to host target binding sites on VGAM102 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM102 host target RNA into VGAM102 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9074] It is appreciated that VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM102 host target genes. The mRNA of each one of this plurality of VGAM102 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM102 RNA, herein designated VGAM RNA, and which when bound by VGAM102 RNA causes inhibition of translation of respective one or more VGAM102 host target proteins.

[9075] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM102 gene, herein designated VGAM GENE, on one or more VGAM102 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9076] It is yet further appreciated that a function of VGAM102 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM102 correlate with, and may be deduced from, the identity of the host target genes which VGAM102 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9077] Nucleotide sequences of the VGAM102 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM102 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM102 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM102 are further described hereinbelow with reference to Table 1.

[9078] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM102 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM102 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9079] As mentioned hereinabove with reference to Fig. 1, a function of VGAM102 gene, herein designated VGAM is inhibition of expression of VGAM102 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM102 correlate with, and may be deduced from, the identity of the target genes which VGAM102 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9080] Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175) is a VGAM102 host target gene. C8orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf2 BINDING SITE, designated SEQ ID:14020, to the

nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, also designated SEQ ID:2813.

[9081] A function of VGAM102 is therefore inhibition of Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175). Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf2. Potassium Channel, Subfamily K, Member 13 (KCNK13, Accession NM_022054) is another VGAM102 host target gene. KCNK13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNK13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK13 BINDING SITE, designated SEQ ID:22592, to the nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, also designated SEQ ID:2813.

[9082] Another function of VGAM102 is therefore inhibition of Potassium Channel, Subfamily K, Member 13 (KCNK13, Accession NM_022054). Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK13. START Domain Containing 7 (STARD7, Accession NM_020151) is

another VGAM102 host target gene. STARD7 BINDING SITE1 and STARD7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STARD7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STARD7 BINDING SITE1 and STARD7 BINDING SITE2, designated SEQ ID:21355 and SEQ ID:29259 respectively, to the nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, also designated SEQ ID:2813.

[9083] Another function of VGAM102 is therefore inhibition of START Domain Containing 7 (STARD7, Accession NM_020151). Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STARD7. LOC57107 (Accession NM_020381) is another VGAM102 host target gene. LOC57107 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57107 BINDING SITE, desig-

nated SEQ ID:21648, to the nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, also designated SEQ ID:2813.

[9084] Another function of VGAM102 is therefore inhibition of LOC57107 (Accession NM_020381). Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57107. LOC90643 (Accession XM_033145) is another VGAM102 host target gene. LOC90643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90643 BINDING SITE, designated SEQ ID:31852, to the nucleotide sequence of VGAM102 RNA, herein designated VGAM RNA, also designated SEQ ID:2813.

[9085] Another function of VGAM102 is therefore inhibition of LOC90643 (Accession XM_033145). Accordingly, utilities of VGAM102 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90643. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 103 (VGAM103) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9086] VGAM103 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM103 was detected is described hereinabove with reference to Figs. 1–8.

[9087] VGAM103 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9088] VGAM103 gene encodes a VGAM103 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM103 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM103 precursor RNA is designated SEQ ID:89, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:89 is located at position 49030 relative to the genome of

Plutella Xylostella Granulovirus.

[9089] VGAM103 precursor RNA folds onto itself, forming VGAM103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9090] An enzyme complex designated DICER COMPLEX, `dices` the VGAM103 folded precursor RNA into VGAM103 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM103 RNA is designated SEQ ID:2814, and is provided hereinbelow with reference to the sequence listing part.

[9091] VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM103 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9092] VGAM103 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM103 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM103 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9093] The complementary binding of VGAM103 RNA, herein designated VGAM RNA, to host target binding sites on VGAM103 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM103 host target RNA into VGAM103 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9094] It is appreciated that VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM103 host target genes. The mRNA of each one of this plurality of VGAM103 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM103 RNA, herein designated VGAM RNA, and which when bound by VGAM103 RNA causes inhibition of translation of respective one or more VGAM103 host target proteins.

[9095] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM103 gene, herein designated VGAM GENE, on one or more VGAM103 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9096] It is yet further appreciated that a function of VGAM103 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of

VGAM103 correlate with, and may be deduced from, the identity of the host target genes which VGAM103 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9097] Nucleotide sequences of the VGAM103 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM103 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM103 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM103 are further described hereinbelow with reference to Table 1.

[9098] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM103 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM103 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9099] As mentioned hereinabove with reference to Fig. 1, a function of VGAM103 gene, herein designated VGAM is inhibition of expression of VGAM103 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM103 correlate with, and may be deduced

from, the identity of the target genes which VGAM103 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9100] ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916) is a VGAM103 host target gene. ATP8A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP8A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8A2 BINDING SITE, designated SEQ ID:44918, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9101] A function of VGAM103 is therefore inhibition of ATPase, Aminophospholipid Transporter-like, Class I, Type 8A, Member 2 (ATP8A2, Accession XM_167916). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8A2. Glucosaminyl (N-acetyl) Transferase 3, Mucin Type (GCNT3, Accession NM_004751) is another VGAM103 host target gene. GCNT3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by GCNT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCNT3 BINDING SITE, designated SEQ ID:11140, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9102] Another function of VGAM103 is therefore inhibition of Glucosaminyl (N-acetyl) Transferase 3, Mucin Type (GCNT3, Accession NM_004751), a gene which catalyzes O-glycan branch synthesis of the core 2 and core 4 type in mucins and controls expression of core 2 branched oligosaccharides and I antigens on the cell surface. Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCNT3. The function of GCNT3 has been established by previous studies. Mucin-type glycoproteins are unique in that they have clusters of O-glycans containing N-acetylgalactosamine residues at reducing ends, which are linked to serine or threonine. O-glycans are classified according to the core structures, which can be converted in the presence of an N-acetylglucosaminyltransferase, such as GCNT3.

- [9103] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9104] Schwientek, T.; Nomoto, M.; Levery, S. B.; Merkx, G.; van Kessel, A. G.; Bennett, E. P.; Hollingsworth, M. A.; Clausen, H. : Control of O-glycan branch formation: molecular cloning of human cDNA encoding a novel beta-1,6-N-acetylglucosaminyltransferase forming core 2 and core 4. J. Biol. Chem. 274: 4504-4512, 1999. ; and
- [9105] Yeh, J.-C.; Ong, E.; Fukuda, M. : Molecular cloning and expression of a novel beta-1,6-N-acetylglucosaminyltransferase that forms core 2, core 4, and I branches. J. Biol. Chem. 274: 321.
- [9106] Further studies establishing the function and utilities of GCNT3 are found in John Hopkins OMIM database record ID 606836, and in cited publications numbered 557 and 12157 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Synaptogyrin 3 (SYNGR3, Accession NM_004209) is another VGAM103 host target gene. SYNGR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR3 BINDING SITE, designated SEQ ID:10409, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9107] Another function of VGAM103 is therefore inhibition of Synaptogyrin 3 (SYNGR3, Accession NM_004209). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR3. Very Low Density Lipoprotein Receptor (VLDLR, Accession XM_045386) is another VGAM103 host target gene. VLDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VLDLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VLDLR BINDING SITE, designated SEQ ID:34450, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9108] Another function of VGAM103 is therefore inhibition of Very Low Density Lipoprotein Receptor (VLDLR, Accession XM_045386), a gene which may play a crucial role in

triglyceride metabolism. Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VLDLR. The function of VLDLR has been established by previous studies. A specific isoform of apolipoprotein E (OMIM Ref. No. 107741), encoded by the APOE4 allele, is associated with the accelerated rate of disease expression of sporadic Alzheimer disease (AD) and late-onset familial AD. Okuizumi et al. (1995) noted that, in patients who carry the APOE4 allele, an earlier age of onset has also been demonstrated in patients who also have mutations in the amyloid precursor protein gene (OMIM Ref. No. 104760) involving codon 717 (104760.0002) and codons 670 and 671 (104760.0008). On the other hand, the presence of the APOE4 allele makes no difference in familial AD patients with APP692 (104760.0005) or APP693 mutations, nor does it make a difference in chromosome 14-linked familial AD patients (OMIM Ref. No. 104311). Hypothesizing that receptors for APOE-containing lipoproteins act as a potential risk factor for AD, Okuizumi et al. (1995) performed an association study using a polymorphic triplet (CGG) repeat in the VLDLR gene. The frequency of the 5-repeat allele was significantly higher in all Japanese

sporadic AD patients (P less than 0.02) than in Japanese controls. Moreover, the odds ratio was significantly increased in the AD patients homozygous for the 5-repeat allele; OR = 2.1, 95% confidence interval = 1.1–4.2. Multiple logistic regression analysis showed that the relative risk conferred by the presence of 2 copies of the 5-repeat allele and at least 1 copy of the APOE4 allele is 8.7; 95% CI = 2.9–25.8. Okuizumi et al. (1995) concluded that VLDLR is a susceptibility gene for AD. Animal model experiments lend further support to the function of VLDLR. Layering of neurons in the cerebral cortex and cerebellum requires reelin (RELN; 600514), an extracellular matrix protein, and mammalian disabled (DAB1; 603448), a cytosolic protein that activates tyrosine kinases. By targeted disruption experiments in mice, Trommsdorff et al. (1999) showed that 2 cell surface receptors, VLDLR and apolipoprotein E receptor-2 (APOER2; 602600), are also required. Both receptors bound Dab1 on their cytoplasmic tails and were expressed in cortical and cerebellar layers adjacent to layers expressing Reln. Dab1 expression was upregulated in knockout mice lacking both the *Vldlr* and *Apoer2* genes. Inversion of cortical layers, absence of cerebellar foliation, and the migration of Purkinje cells in these animals pre-

cisely mimicked the phenotype of mice lacking Reln or Dab1. These findings established novel signaling functions for the LDL receptor gene family and suggested that VLDLR and APOER2 participate in transmitting the extracellular RELN signal to intracellular signaling processes initiated by DAB1.

[9109] It is appreciated that the abovementioned animal model for VLDLR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9110] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9111] Okuizumi, K.; Onodera, O.; Namba, Y.; Ikeda, K.; Yamamoto, T.; Seki, K.; Ueki, A.; Nanko, S.; Tanaka, H.; Takahashi, H.; Oyanagi, K.; Mizusawa, H.; Kanazawa, I.; Tsuji, S. : Genetic association of the very low density lipoprotein (VLDL) receptor gene with sporadic Alzheimer's disease. *Nature Genet.* 11: 207–209, 1995. ; and

[9112] Trommsdorff, M.; Gotthardt, M.; Hiesberger, T.; Shelton, J.; Stockinger, W.; Nimpf, J.; Hammer, R. E.; Richardson, J. A.; Herz, J. : Reeler/Disabled-like disruption of neuronal

migration.

[9113] Further studies establishing the function and utilities of VLDLR are found in John Hopkins OMIM database record ID 192977, and in cited publications numbered 10022, 10020–10021, 80 and 10023–10024 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916) is another VGAM103 host target gene. AP1S2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1S2 BINDING SITE, designated SEQ ID:10000, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9114] Another function of VGAM103 is therefore inhibition of Adaptor-related Protein Complex 1, Sigma 2 Subunit (AP1S2, Accession NM_003916). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1S2. BTB (POZ) Domain Containing 3 (BTBD3, Accession

NM_014962) is another VGAM103 host target gene.

BTBD3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17336, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9115] Another function of VGAM103 is therefore inhibition of BTB (POZ) Domain Containing 3 (BTBD3, Accession NM_014962). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. FLJ10290 (Accession NM_018047) is another VGAM103 host target gene. FLJ10290 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10290 BINDING SITE, designated SEQ ID:19796, to the nucleotide sequence of VGAM103

RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9116] Another function of VGAM103 is therefore inhibition of FLJ10290 (Accession NM_018047). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10290. FLJ20079 (Accession NM_017656) is another VGAM103 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19178, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9117] Another function of VGAM103 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. FLJ20695 (Accession NM_017929) is another VGAM103 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ20695, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19612, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9118] Another function of VGAM103 is therefore inhibition of FLJ20695 (Accession NM_017929). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. HOMER-2B (Accession NM_004839) is another VGAM103 host target gene. HOMER-2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOMER-2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOMER-2B BINDING SITE, designated SEQ ID:11246, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9119] Another function of VGAM103 is therefore inhibition of HOMER-2B (Accession NM_004839). Accordingly, utilities

of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOMER-2B. KIAA1871 (Accession XM_028409) is another VGAM103 host target gene. KIAA1871 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1871 BINDING SITE, designated SEQ ID:30708, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9120] Another function of VGAM103 is therefore inhibition of KIAA1871 (Accession XM_028409). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1871. Yes-associated Protein 1, 65kDa (YAP1, Accession NM_006106) is another VGAM103 host target gene. YAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of YAP1 BINDING SITE, designated SEQ ID:12754, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9121] Another function of VGAM103 is therefore inhibition of Yes-associated Protein 1, 65kDa (YAP1, Accession NM_006106). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP1. LOC221477 (Accession XM_166397) is another VGAM103 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44251, to the nucleotide sequence of VGAM103 RNA, herein designated VGAM RNA, also designated SEQ ID:2814.

[9122] Another function of VGAM103 is therefore inhibition of LOC221477 (Accession XM_166397). Accordingly, utilities of VGAM103 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 104 (VGAM104) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9123] VGAM104 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM104 was detected is described hereinabove with reference to Figs. 1–8.

[9124] VGAM104 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9125] VGAM104 gene encodes a VGAM104 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM104 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM104 precursor RNA is designated SEQ ID:90, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:90 is

located at position 67576 relative to the genome of
Plutella Xylostella Granulovirus.

[9126] VGAM104 precursor RNA folds onto itself, forming VGAM104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9127] An enzyme complex designated DICER COMPLEX, `dices` the VGAM104 folded precursor RNA into VGAM104 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM104 RNA is designated SEQ ID:2815, and is provided hereinbelow with reference to the sequence listing part.

[9128] VGAM104 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM104 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9129] VGAM104 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM104 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM104 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM104 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[9130] The complementary binding of VGAM104 RNA, herein designated VGAM RNA, to host target binding sites on VGAM104 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM104 host target RNA into VGAM104 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9131] It is appreciated that VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM104 host target genes. The mRNA of each one of this plurality of VGAM104 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM104 RNA, herein designated VGAM RNA, and which when bound by VGAM104 RNA causes inhibition of translation of respective one or more VGAM104

host target proteins.

[9132] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM104 gene, herein designated VGAM GENE, on one or more VGAM104 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9133] It is yet further appreciated that a function of VGAM104 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM104 include diagnosis, prevention and treatment of viral infection by *Plutella Xylostella* Gran-

ulovirus. Specific functions, and accordingly utilities, of VGAM104 correlate with, and may be deduced from, the identity of the host target genes which VGAM104 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [9134] Nucleotide sequences of the VGAM104 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM104 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM104 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM104 are further described hereinbelow with reference to Table 1.
- [9135] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM104 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM104 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [9136] As mentioned hereinabove with reference to Fig. 1, a function of VGAM104 gene, herein designated VGAM is inhibition of expression of VGAM104 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM104 correlate with, and may be deduced from, the identity of the target genes which VGAM104 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9137] Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418) is a VGAM104 host target gene. C11orf25 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by C11orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf25 BINDING SITE, designated SEQ ID:25397, to the nucleotide sequence of VGAM104 RNA, herein designated VGAM RNA, also designated SEQ ID:2815.

[9138] A function of VGAM104 is therefore inhibition of Chromosome 11 Open Reading Frame 25 (C11orf25, Accession NM_031418). Accordingly, utilities of VGAM104 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf25. LOC150142 (Accession XM_086791) is another VGAM104 host target gene. LOC150142 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded

by LOC150142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150142 BINDING SITE, designated SEQ ID:38847, to the nucleotide sequence of VGAM104 RNA, herein designated VGAM RNA, also designated SEQ ID:2815.

[9139] Another function of VGAM104 is therefore inhibition of LOC150142 (Accession XM_086791). Accordingly, utilities of VGAM104 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150142. LOC200982 (Accession XM_117305) is another VGAM104 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43371, to the nucleotide sequence of VGAM104 RNA, herein designated VGAM RNA, also designated SEQ ID:2815.

[9140] Another function of VGAM104 is therefore inhibition of LOC200982 (Accession XM_117305). Accordingly, utilities

of VGAM104 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 105 (VGAM105) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9141] VGAM105 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM105 was detected is described hereinabove with reference to Figs. 1–8.

[9142] VGAM105 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Plutella Xylostella Granulovirus. VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9143] VGAM105 gene encodes a VGAM105 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM105 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM105 precursor RNA is designated SEQ ID:91, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:91 is located at position 89565 relative to the genome of *Plutella Xylostella Granulovirus*.

[9144] VGAM105 precursor RNA folds onto itself, forming VGAM105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9145] An enzyme complex designated DICER COMPLEX, `dices` the VGAM105 folded precursor RNA into VGAM105 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM105 RNA is designated SEQ ID:2816, and

is provided hereinbelow with reference to the sequence listing part.

[9146] VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM105 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9147] VGAM105 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM105 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM105 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9148] The complementary binding of VGAM105 RNA, herein designated VGAM RNA, to host target binding sites on VGAM105 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM105 host target RNA into VGAM105 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9149] It is appreciated that VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM105 host target genes. The mRNA of each one of this plurality of VGAM105 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM105 RNA, herein designated VGAM RNA, and which when bound by VGAM105 RNA causes inhibition of translation of respective one or more VGAM105 host target proteins.

[9150] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM105 gene, herein designated VGAM GENE, on one or more VGAM105 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9151] It is yet further appreciated that a function of VGAM105 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM105 include diagnosis, prevention and treatment of viral infection by Plutella Xylostella Granulovirus. Specific functions, and accordingly utilities, of VGAM105 correlate with, and may be deduced from, the identity of the host target genes which VGAM105 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9152] Nucleotide sequences of the VGAM105 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM105 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM105 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM105 are further described hereinbelow with reference to Table 1.

[9153] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM105 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM105 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9154] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM105 gene, herein designated VGAM is inhibition of expression of VGAM105 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM105 correlate with, and may be deduced from, the identity of the target genes which VGAM105 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9155] FLJ10292 (Accession NM_018048) is a VGAM105 host target gene. FLJ10292 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10292 BINDING SITE, designated SEQ ID:19801, to the nucleotide sequence of VGAM105 RNA, herein designated VGAM RNA, also designated SEQ ID:2816.

[9156] A function of VGAM105 is therefore inhibition of FLJ10292 (Accession NM_018048). Accordingly, utilities of VGAM105 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10292. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present inven-

tion, referred to here as Viral Genomic Address Messenger 106 (VGAM106) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9157] VGAM106 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM106 was detected is described hereinabove with reference to Figs. 1–8.

[9158] VGAM106 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9159] VGAM106 gene encodes a VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM106 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM106 precursor RNA is designated SEQ ID:92, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:92 is located at position 49997 relative to the genome of Saimiriine Herpesvirus 2.

[9160] VGAM106 precursor RNA folds onto itself, forming VGAM106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9161] An enzyme complex designated DICER COMPLEX, `dices` the VGAM106 folded precursor RNA into VGAM106 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM106 RNA is designated SEQ ID:2817, and is provided hereinbelow with reference to the sequence listing part.

[9162] VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM106 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM106 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9163] VGAM106 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM106 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM106 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9164] The complementary binding of VGAM106 RNA, herein designated VGAM RNA, to host target binding sites on VGAM106 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM106 host target RNA into VGAM106 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9165] It is appreciated that VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM106 host target genes. The mRNA of each one of this plurality of VGAM106 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM106 RNA, herein designated VGAM RNA, and which when bound by VGAM106 RNA causes inhibition of translation of respective one or more VGAM106 host target proteins.

[9166] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM106 gene, herein designated VGAM GENE, on one or more VGAM106 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9167] It is yet further appreciated that a function of VGAM106 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM106 correlate with, and may be deduced from, the identity of

the host target genes which VGAM106 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9168] Nucleotide sequences of the VGAM106 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM106 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM106 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM106 are further described hereinbelow with reference to Table 1.

[9169] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM106 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM106 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9170] As mentioned hereinabove with reference to Fig. 1, a function of VGAM106 gene, herein designated VGAM is inhibition of expression of VGAM106 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM106 correlate with, and may be deduced from, the identity of the target genes which VGAM106

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9171] Inositol 1,4,5-triphosphate Receptor, Type 1 (ITPR1, Accession NM_002222) is a VGAM106 host target gene. ITPR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR1 BINDING SITE, designated SEQ ID:7986, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9172] A function of VGAM106 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 1 (ITPR1, Accession NM_002222), a gene which couples cell membrane receptors to Ca^{2+} signal transduction pathways. Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR1. The function of ITPR1 has been established by previous studies. Inositol 1,4,5-triphosphate is an intracellular second messenger produced by phospholipase C through a G protein-dependent mechanism. It releases calcium from endoplasmic reticulum by binding to specific

receptors that are coupled to calcium channels. These receptors are abundant in neuronal and nonneuronal tissues. The neuronal form of the receptor is abundant in the cerebellum, particularly the perikaryon of the Purkinje cells. Matsumoto et al. (1996) noted that the product of the ITPR1 gene is predominantly enriched in cerebellar Purkinje cells but is also concentrated in neurons in the hippocampal CA1 region, caudate-putamen, and cerebral cortex. The inositol triphosphate receptor shares sequence and functional homology with the ryanodine receptor (OMIM Ref. No. 180901); they both trigger the release of calcium from intracellular stores. The primary structure of the inositol triphosphate receptor contains 3 domains: an inositol triphosphate binding domain near the N terminus, a coupling domain in the middle of the molecule, and a transmembrane spanning domain near the C terminus. In addition, there are at least 2 consensus protein kinase A phosphorylation sites and at least 1 consensus ATP-binding site (Nucifora et al., 1995). Matsumoto et al. (1996) found that most ITPR1-deficient mice generated by gene targeting die in utero, and that most animals that are born alive have severe ataxia and tonic or tonic-clonic seizures and die by the weaning period. Elec-

troencephalograms showed that they suffer from epilepsy, indicating that ITPR1 is essential for proper brain function. However, observation by light microscope of the hematoxylin–eosin staining of the brain and peripheral tissues of deficient mice showed no abnormality and the unique electrophysiologic properties of the cerebellar Purkinje cells of deficient mice were not severely impaired. In the mouse the *Intp3r* locus is closely situated to the 'opisthotonus' mutant locus (*opt*), and *Opt* homozygous mutant mice exhibit phenotypes similar to those described for the knockout mice. The *opt* locus is on mouse chromosome 6

[9173] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9174] Matsumoto, M.; Nakagawa, T.; Inoue, T.; Nagata, E.; Tanaka, K.; Takano, H.; Minowa, O.; Kuno, J.; Sakakibara, S.; Yamada, M.; Yoneshima, H.; Miyawaki, A; Fukuichi, T.; Furuichi, T.; Okano, H.; Mikoshiba, K.; Noda, T. : Ataxia and epileptic seizures in mice lacking type 1 inositol 1,4,5–triphosphate receptor. *Nature* 379: 168–171, 1996.
; and

[9175] Nucifora, F. C., Jr.; Li, S.–H.; Danoff, S.; Ullrich, A.; Ross, C. A. : Molecular cloning of a cDNA for the human inositol

1,4,5-trisphosphate receptor type 1, and the identification of.

[9176] Further studies establishing the function and utilities of ITPR1 are found in John Hopkins OMIM database record ID 147265, and in cited publications numbered 4976–4977, 481 and 4820 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Matrix Metalloproteinase 19 (MMP19, Accession NM_002429) is another VGAM106 host target gene. MMP19 BINDING SITE1 and MMP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE1 and MMP19 BINDING SITE2, designated SEQ ID:8267 and SEQ ID:23074 respectively, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9177] Another function of VGAM106 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_002429). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with MMP19. Chromosome 9 Open Reading Frame 5 (C9orf5, Accession NM_032012) is another VGAM106 host target gene. C9orf5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C9orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C9orf5 BINDING SITE, designated SEQ ID:25717, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9178] Another function of VGAM106 is therefore inhibition of Chromosome 9 Open Reading Frame 5 (C9orf5, Accession NM_032012). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C9orf5. Di-Ras2 (Accession NM_017594) is another VGAM106 host target gene. Di-Ras2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by Di-Ras2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Di-Ras2 BINDING SITE, designated SEQ

ID:19042, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9179] Another function of VGAM106 is therefore inhibition of Di-Ras2 (Accession NM_017594). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Di-Ras2. DKFZP434P211 (Accession NM_014549) is another VGAM106 host target gene. DKFZP434P211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P211 BINDING SITE, designated SEQ ID:15865, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9180] Another function of VGAM106 is therefore inhibition of DKFZP434P211 (Accession NM_014549). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P211. FLJ23017 (Accession NM_022840) is another VGAM106 host target gene. FLJ23017 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23017, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23017 BINDING SITE, designated SEQ ID:23128, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9181] Another function of VGAM106 is therefore inhibition of FLJ23017 (Accession NM_022840). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23017. KIAA0523 (Accession XM_041964) is another VGAM106 host target gene. KIAA0523 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0523 BINDING SITE, designated SEQ ID:33644, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9182] Another function of VGAM106 is therefore inhibition of

KIAA0523 (Accession XM_041964). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0523. KIAA1046 (Accession NM_014928) is another VGAM106 host target gene. KIAA1046 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1046 BINDING SITE, designated SEQ ID:17221, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9183] Another function of VGAM106 is therefore inhibition of KIAA1046 (Accession NM_014928). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1046. Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM_002714) is another VGAM106 host target gene. PPP1R10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP1R10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R10 BINDING SITE, designated SEQ ID:8578, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9184] Another function of VGAM106 is therefore inhibition of Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM_002714). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R10. SEC15B (Accession XM_039570) is another VGAM106 host target gene. SEC15B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC15B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC15B BINDING SITE, designated SEQ ID:33126, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9185] Another function of VGAM106 is therefore inhibition of SEC15B (Accession XM_039570). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SEC15B. Translocase of Inner Mitochondrial Membrane 9 Homolog (yeast) (TIMM9, Accession NM_012460) is another VGAM106 host target gene. TIMM9 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TIMM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIMM9 BINDING SITE, designated SEQ ID:14831, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9186] Another function of VGAM106 is therefore inhibition of Translocase of Inner Mitochondrial Membrane 9 Homolog (yeast) (TIMM9, Accession NM_012460). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIMM9. LOC150174 (Accession XM_086802) is another VGAM106 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of
LOC150174 BINDING SITE, designated SEQ ID:38872, to
the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9187] Another function of VGAM106 is therefore inhibition of LOC150174 (Accession XM_086802). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. LOC150213 (Accession XM_059324) is another VGAM106 host target gene. LOC150213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150213 BINDING SITE, designated SEQ ID:36956, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9188] Another function of VGAM106 is therefore inhibition of LOC150213 (Accession XM_059324). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150213. LOC152313 (Accession XM_098190) is another VGAM106 host target gene. LOC152313 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152313 BINDING SITE, designated SEQ ID:41472, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9189] Another function of VGAM106 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC201965 (Accession XM_114412) is another VGAM106 host target gene. LOC201965 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201965, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201965 BINDING SITE, designated SEQ ID:42934, to the nucleotide sequence of VGAM106 RNA, herein designated VGAM RNA, also designated SEQ ID:2817.

[9190] Another function of VGAM106 is therefore inhibition of LOC201965 (Accession XM_114412). Accordingly, utilities of VGAM106 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC201965. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 107 (VGAM107) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9191] VGAM107 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM107 was detected is described hereinabove with reference to Figs. 1–8.

[9192] VGAM107 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9193] VGAM107 gene encodes a VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM107 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM107 precursor RNA is designated SEQ ID:93, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:93 is located at position 50521 relative to the genome of Saimiriine Herpesvirus 2.

[9194] VGAM107 precursor RNA folds onto itself, forming VGAM107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9195] An enzyme complex designated DICER COMPLEX, `dices` the VGAM107 folded precursor RNA into VGAM107 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM107 RNA is designated SEQ ID:2818, and is provided hereinbelow with reference to the sequence listing part.

[9196] VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM107 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9197] VGAM107 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM107 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM107 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[9198] The complementary binding of VGAM107 RNA, herein designated VGAM RNA, to host target binding sites on VGAM107 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM107 host target RNA into VGAM107 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9199] It is appreciated that VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM107 host target genes. The mRNA of each one of this plurality of VGAM107 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM107 RNA, herein designated VGAM RNA, and which when bound by VGAM107 RNA causes in-

hibition of translation of respective one or more VGAM107 host target proteins.

[9200] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM107 gene, herein designated VGAM GENE, on one or more VGAM107 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9201] It is yet further appreciated that a function of VGAM107 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM107 include diagnosis, prevention and

treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM107 correlate with, and may be deduced from, the identity of the host target genes which VGAM107 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9202] Nucleotide sequences of the VGAM107 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM107 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM107 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM107 are further described hereinbelow with reference to Table 1.

[9203] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM107 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM107 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9204] As mentioned hereinabove with reference to Fig. 1, a function of VGAM107 gene, herein designated VGAM is inhibition of expression of VGAM107 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM107 correlate with, and may be deduced from, the identity of the target genes which VGAM107 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9205] Epithelial Membrane Protein 1 (EMP1, Accession NM_001423) is a VGAM107 host target gene. EMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EMP1 BINDING SITE, designated SEQ ID:7134, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9206] A function of VGAM107 is therefore inhibition of Epithelial Membrane Protein 1 (EMP1, Accession NM_001423), a gene which plays a role in squamous cell differentiation; member of the PMP22/EMP/MP20 family of membrane glycoproteins. Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EMP1. The function of EMP1 has been established by previous studies. Ben-Porath and

Benvenisty (1996) cloned a cDNA encoding epithelial membrane protein-1 (EMP1), named TMP by them, using RT-PCR on human embryo kidney RNA. Ruegg et al. (1996) independently isolated a cDNA encoding EMP1, termed B4B by them, using differential display PCR. The predicted 157-amino acid EMP1 protein contains 4 trans-membrane domains and 2 potential N-linked glycosylation sites in the first extracellular loop. Chen et al. (1997) found that EMP1, named CL-20 by them, shares 39% amino acid identity with peripheral myelin protein-22 (PMP22; 601097); the conserved amino acids are located predominantly within the membrane-spanning domains. Due to the high amino acid sequence homology among PMP22, EMP1, EMP2 (OMIM Ref. No. 602334), and EMP3 (OMIM Ref. No. 602335), Ben-Porath and Benvenisty (1996) proposed that these proteins are members of a novel family. Based on the suggested functions of PMP22, they proposed that EMP1 is involved in cell-cell interactions and the control of cell proliferation. Chen et al. (1997) found that the EMP1 gene contains 5 exons and 4 introns, and they noted that the exon/intron junctions are located at the same positions as those of PMP22, suggesting that EMP1 and PMP22 arose by duplication of a com-

mon ancestral gene. Using Northern blot analysis, they detected a 2.8-kb EMP1 transcript in most of the adult tissues examined, but not in brain, liver, pancreas, or peripheral blood leukocytes. Using RT-PCR, Ben-Porath and Benvenisty (1996) detected EMP1 expression in embryonic kidney, brain, and gut, but not in liver and thymus. Marvin et al. (1995) localized the EMP1 gene to chromosome 12 using a somatic cell hybrid panel. By fluorescence in situ hybridization, Chen et al. (1997) and Ruegg et al. (1996) mapped the EMP1 gene to 12p12 and 20q12-q13.1, respectively. By FISH, somatic cell hybridization, and radiation hybrid analysis, Liehr et al. (1999) confirmed assignment of the EMP1 gene to chromosome 12p12.3. Ben Porath et al. (1998) mapped the homologous gene in the mouse to chromosome 6.

[9207] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9208] Ben Porath, I.; Kozak, C. A.; Benvenisty, N. : Chromosomal mapping of Tmp (Emp1), Xmp (Emp2), and Ymp (Emp3), genes encoding membrane proteins related to Pmp22. Genomics 49: 443-447, 1998. ; and

[9209] Chen, Y.; Medvedev, A.; Ruzanov, P.; Marvin, K. W.; Jetten,

A. M. : cDNA cloning, genomic structure, and chromosome mapping of the human epithelial membrane protein CL-20 gene (EMP1), a.

[9210] Further studies establishing the function and utilities of EMP1 are found in John Hopkins OMIM database record ID 602333, and in cited publications numbered 9305-6011 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM_001315) is another VGAM107 host target gene. MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPK14, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3, designated SEQ ID:7000, SEQ ID:29111 and SEQ ID:29104 respectively, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9211] Another function of VGAM107 is therefore inhibition of Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM_001315), a gene which is important for cytokine pro-

duction; responds to changes in extracellular osmolarity. Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK14. The function of MAPK14 has been established by previous studies. Tamura et al. (2000) investigated a role for Mapk14 in mouse development and physiology by targeted disruption of the Mapk14 gene. Whereas some Mapk14 $-/-$ embryos died between embryonic days 11.5 and 12.5, those that developed past this stage had normal morphology but were anemic, owing to failed definitive erythropoiesis caused by diminished expression of the erythropoietin gene (EPO; 133170). Since Mapk14-deficient hematopoietic stem cells reconstituted lethally irradiated hosts, Mapk14 function is not required downstream of the Epo receptor (EPOR; 133171). Inhibition of MAPK14 activity also interfered with stabilization of EPO mRNA in human hepatoma cells undergoing hypoxic stress. The authors concluded that MAPK14 plays a critical role linking developmental and stress-induced erythropoiesis through regulation of EPO expression. Using a yeast 2-hybrid screen of gastrointestinal tract tissue with p38-alpha as the bait, Ge et al. (2002) isolated multiple clones encoding TAB1 (OMIM Ref. No. 602615). Im-

munoprecipitation and GST pull-down analyses indicated that TAB1 interacts with p38- α , but not with other MAPKs, with or without treatment with TNF. Immunoblot analysis showed that coexpression of TAB1 and p38- α enhanced autophosphorylation of p38- α even in the presence of dominant-negative forms of MAP2Ks (e.g., MAP2K3; 602315) and TAK1 (MAP3K7; 602614). The amino acids between positions 373 and 418 of TAB1 were found to be required for phosphorylation of p38- α . Expression of TLR2 (OMIM Ref. No. 603028) caused p38- α phosphorylation in the presence or absence of inhibitors, whereas p38- α phosphorylation after stimulation of TLR4 (OMIM Ref. No. 603030) could be inhibited by mutant TAB1, suggesting that activation of p38- α can be TAB1 dependent or independent. Immunoblot analysis detected the formation of TRAF6 (OMIM Ref. No. 602355)-TAB1-p38- α complexes. Formation of these complexes could be enhanced by stimulation with lipopolysaccharide. Ge et al. (2002) concluded that activation of p38- α by a nonenzymatic adaptor protein such as TAB1 may be an important alternative activation pathway operating in parallel with kinase cascades in regulating intracellular signaling

- [9212] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9213] Tamura, K.; Sudo, T.; Senftleben, U.; Dadak, A. M.; Johnson, R.; Karin, M. : Requirement for p38-alpha in erythropoietin expression: a role for stress kinases in erythropoiesis. Cell 102: 221-231, 2000. ; and
- [9214] Ge, B.; Gram, H.; Di Padova, F.; Huang, B.; New, L.; Ulevitch, R. J.; Luo, Y.; Han, J. : MAPKK-independent activation of p38-alpha mediated by TAB1-dependent autophosphorylation of p38- α .
- [9215] Further studies establishing the function and utilities of MAPK14 are found in John Hopkins OMIM database record ID 600289, and in cited publications numbered 10123, 10124, 10125-1013 and 11101 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM107 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SYNGR1 BINDING SITE, designated SEQ ID:11058, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9216] Another function of VGAM107 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 has been established by previous studies. Rat synaptogyrin, or RAT-SYNGR1, is an integral membrane protein associated with presynaptic vesicles in neuronal cells. See SYNGR2 (OMIM Ref. No. 603926). As part of an effort to sequence the long arm of human chromosome 22, Kedra et al. (1998) identified the human homolog of RATSNGR1, synaptogyrin-1 (OMIM Ref. No. SYNGR1). By a combination of EST database searching and library screening, the authors isolated cDNAs corresponding to 3 alternatively spliced transcripts, which they designated SYNGR1a-c. The predicted 1a, 1b, and 1c proteins contain 234, 191, and 192 amino acids, respectively. Northern blot analysis revealed that

the 4.5-kb SYNGR1a mRNA is expressed at high levels in brain. The other transcript forms are expressed at low levels in nonneuronal tissues. In situ hybridization to embryonic and adult mouse tissues confirmed that SYNGR1a, the most abundant transcript form, shows predominantly neuronal expression. Kedra et al. (1998) also identified cDNAs encoding the related human proteins SYNGR2 and SYNGR3 (OMIM Ref. No. 603927) and mouse *Syng1b*. Like RATSNGR1, the mouse and human synaptogyrin family members contain 4 membrane-spanning domains. The conserved central portion of SYNGR1a shares 54%, 61%, and 92% identity with that of SYNGR2, SYNGR3, and RATSNGR1, respectively. Animal model experiments lend further support to the function of SYNGR1. Using gene targeting, Janz et al. (1999) generated mice lacking *Syng1*. They bred these *Syng1* knockout mice against *Syp* (OMIM Ref. No. 313475) knockout mice generated by McMahon et al. (1996) to create double knockout mice deficient in both *Syp* and *Syng1*. Both single and double knockout mice were viable and fertile. Morphologic and biochemical analysis showed that the architecture and composition of synapses were unaltered in the brains of *Syng1* single knockout and *Syng1/Syp* double knockout

mutant mice. Electrophysiologic recordings in the hippocampal CA1 region revealed that short- and long-term synaptic plasticity was severely reduced in the Syngn1/Syp double knockout mice without changes in the fundamental release apparatus, vesicle cycling, or release probability. Janz et al. (1999) concluded that Syngn1 and Syp perform essential and redundant functions in synaptic plasticity without being required for synaptic transmission as such.

[9217] It is appreciated that the abovementioned animal model for SYNGR1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9218] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9219] Janz, R.; Sudhof, T. C.; Hammer, R. E.; Unni, V.; Siegelbaum, S. A.; Bolshakov, V. Y. : Essential roles in synaptic plasticity for synaptogyrin I and synaptophysin I. *Neuron* 24: 687–700, 1999. ; and

[9220] Kedra, D.; Pan, H.-Q.; Seroussi, E.; Fransson, I.; Guilbaud, C.; Collins, J. E.; Dunham, I.; Blennow, E.; Roe, B. A.; Piehl, F.; Dumanski, J. P. : Characterization of the human

synapto.

[9221] Further studies establishing the function and utilities of SYNGR1 are found in John Hopkins OMIM database record ID 603925, and in cited publications numbered 815 and 8157 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723) is another VGAM107 host target gene. ARHGEF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF2 BINDING SITE, designated SEQ ID:11092, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9222] Another function of VGAM107 is therefore inhibition of Rho/rac Guanine Nucleotide Exchange Factor (GEF) 2 (ARHGEF2, Accession NM_004723). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF2. Bladder Cancer Associated Protein (BLCAP, Ac-

cession NM_006698) is another VGAM107 host target gene. BLCAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BLCAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLCAP BINDING SITE, designated SEQ ID:13520, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9223] Another function of VGAM107 is therefore inhibition of Bladder Cancer Associated Protein (BLCAP, Accession NM_006698). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLCAP. FLJ14800 (Accession NM_032840) is another VGAM107 host target gene. FLJ14800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14800 BINDING SITE, designated SEQ ID:26622, to the nucleotide sequence of VGAM107 RNA,

herein designated VGAM RNA, also designated SEQ ID:2818.

[9224] Another function of VGAM107 is therefore inhibition of FLJ14800 (Accession NM_032840). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14800. HSPC019 (Accession NM_014028) is another VGAM107 host target gene. HSPC019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC019 BINDING SITE, designated SEQ ID:15251, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9225] Another function of VGAM107 is therefore inhibition of HSPC019 (Accession NM_014028). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC019. KIAA1729 (Accession XM_114418) is another VGAM107 host target gene. KIAA1729 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by KIAA1729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1729 BINDING SITE, designated SEQ ID:42947, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9226] Another function of VGAM107 is therefore inhibition of KIAA1729 (Accession XM_114418). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1729. Olfactomedin 3 (OLFM3, Accession XM_088951) is another VGAM107 host target gene. OLFM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OLFM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLFM3 BINDING SITE, designated SEQ ID:39959, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9227] Another function of VGAM107 is therefore inhibition of

Olfactomedin 3 (OLFM3, Accession XM_088951). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLFM3. PAS Domain Containing Serine/threonine Kinase (PASK, Accession NM_015148) is another VGAM107 host target gene. PASK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PASK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PASK BINDING SITE, designated SEQ ID:17501, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9228] Another function of VGAM107 is therefore inhibition of PAS Domain Containing Serine/threonine Kinase (PASK, Accession NM_015148). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PASK. LOC253613 (Accession XM_171225) is another VGAM107 host target gene. LOC253613 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253613, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253613 BINDING SITE, designated SEQ ID:46007, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9229] Another function of VGAM107 is therefore inhibition of LOC253613 (Accession XM_171225). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253613. LOC90092 (Accession XM_028862) is another VGAM107 host target gene. LOC90092 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90092 BINDING SITE, designated SEQ ID:30789, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9230] Another function of VGAM107 is therefore inhibition of LOC90092 (Accession XM_028862). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC90092. LOC91748 (Accession XM_040343) is another VGAM107 host target gene. LOC91748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91748 BINDING SITE, designated SEQ ID:33287, to the nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9231] Another function of VGAM107 is therefore inhibition of LOC91748 (Accession XM_040343). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91748. LOC92249 (Accession XM_043814) is another VGAM107 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34019, to the

nucleotide sequence of VGAM107 RNA, herein designated VGAM RNA, also designated SEQ ID:2818.

[9232] Another function of VGAM107 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM107 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 108 (VGAM108) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9233] VGAM108 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM108 was detected is described hereinabove with reference to Figs. 1–8.

[9234] VGAM108 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9235] VGAM108 gene encodes a VGAM108 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM108 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM108 precursor RNA is designated SEQ ID:94, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:94 is located at position 50791 relative to the genome of Saimiriine Herpesvirus 2.

[9236] VGAM108 precursor RNA folds onto itself, forming VGAM108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9237] An enzyme complex designated DICER COMPLEX, `dices` the VGAM108 folded precursor RNA into VGAM108 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM108 RNA is designated SEQ ID:2819, and is provided hereinbelow with reference to the sequence listing part.

[9238] VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM108 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9239] VGAM108 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM108 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM108 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9240] The complementary binding of VGAM108 RNA, herein designated VGAM RNA, to host target binding sites on VGAM108 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM108 host target RNA into VGAM108 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9241] It is appreciated that VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM108 host target genes. The mRNA of each one of this plurality of VGAM108 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM108 RNA, herein designated VGAM RNA, and which when bound by VGAM108 RNA causes inhibition of translation of respective one or more VGAM108 host target proteins.

[9242] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM108 gene, herein designated VGAM GENE, on one or more VGAM108 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[9243] It is yet further appreciated that a function of VGAM108 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM108 correlate with, and may be deduced from, the identity of the host target genes which VGAM108 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9244] Nucleotide sequences of the VGAM108 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM108 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM108 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM108 are further described hereinbelow with reference to Table 1.

[9245] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM108 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM108 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9246] As mentioned hereinabove with reference to Fig. 1, a function of VGAM108 gene, herein designated VGAM is inhibition of expression of VGAM108 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM108 correlate with, and may be deduced from, the identity of the target genes which VGAM108 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9247] Adenylate Cyclase 7 (ADCY7, Accession NM_001114) is a VGAM108 host target gene. ADCY7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY7 BINDING SITE, designated SEQ ID:6782, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9248] A function of VGAM108 is therefore inhibition of Adenylate Cyclase 7 (ADCY7, Accession NM_001114), a gene

which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY7. The function of ADCY7 has been established by previous studies. Hellevuo et al. (1993) identified a novel form of human adenylyl cyclase (ADCY7) in the human erythroleukemia cell line HEL. It appeared that ADCY7 is the major form of adenylyl cyclase in human platelets. Hellevuo et al. (1995) used PCR techniques in the study of human/rodent somatic hybrid panels and a YAC library to demonstrate that the ADCY7 gene is located on 16q12-q13. The adenylyl cyclase enzyme family is characterized by the presence of 12 membrane-spanning domains in its sequences, and this region of the genome is known to contain other genes encoding proteins characterized by 12 membrane-spanning domains: norepinephrine transporter protein-1 (NET1; 163970), located at 16q12.2, and renal sodium-glucose transporter-2 (SGLT2; 182381), located at 16p11.2.

[9249] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9250] Hellevuo, K.; Berry, R.; Sikela, J. M.; Tabakoff, B. : Local-

ization of the gene for a novel human adenylyl cyclase (ADCY7) to chromosome 16. Hum. Genet. 95: 197–200, 1995. ; and

[9251] Hellevuo, K.; Yoshimura, M.; Kao, M.; Hoffman, P. L.; Cooper, D. M. F.; Tabakoff, B. : A novel adenylyl cyclase sequence cloned from the human erythroleukemia cell line. Biochem. Biophys.

[9252] Further studies establishing the function and utilities of ADCY7 are found in John Hopkins OMIM database record ID 600385, and in cited publications numbered 10690–10691 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB4A, Member RAS Oncogene Family (RAB4A, Accession NM_004578) is another VGAM108 host target gene. RAB4A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB4A BINDING SITE, designated SEQ ID:10925, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9253] Another function of VGAM108 is therefore inhibition of RAB4A, Member RAS Oncogene Family (RAB4A, Accession NM_004578), a gene which is involved in protein transport. Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB4A. The function of RAB4A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Transcriptional Intermediary Factor 1 (TIF1, Accession XM_016701) is another VGAM108 host target gene. TIF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIF1 BINDING SITE, designated SEQ ID:30276, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9254] Another function of VGAM108 is therefore inhibition of Transcriptional Intermediary Factor 1 (TIF1, Accession XM_016701), a gene which mediates the activation function (AF-2) of nuclear estrogen receptor. Accordingly,

utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIF1. The function of TIF1 has been established by previous studies. Hormonal regulation of gene activity is mediated by nuclear receptors acting as ligand-activated transcription factors. The activity of the ligand-dependent activation function, or AF2, of the receptors requires intermediary factors that interact with the AF2-activating domain, a C-terminal region that is highly conserved in the nuclear receptor family. Thenot et al. (1997) isolated human breast cancer cell cDNAs that encode transcription intermediary factor-1 (TIF1), a protein that is able to bind to the AF2-activating domain of the estrogen receptor (ESR; e.g., 133430). The deduced 1,013-amino acid TIF1 protein, which is more than 92% conserved with mouse Tif1, contains several domains: a RING finger, B-box fingers, a coiled-coil domain, a PHD homeodomain finger, and a bromodomain. A 26-amino acid region of TIF1 is sufficient for its hormone-dependent binding to the ESR. Thenot et al. (1997) demonstrated that the AF2-activating domain of ESR is required but not sufficient for the binding of TIF1, that TIF1 association with DNA-bound ESR requires the presence of estradiol, and that TIF1 interacts

selectively with different nuclear receptors. The authors identified a cDNA variant that encodes a TIF1 isoform containing a 34-amino acid insertion. Northern blot analysis detected a major 4.5-kb transcript in MCF7 breast cancer cells. Fusion of PML (OMIM Ref. No. 102578) and TIF1A to RARA (OMIM Ref. No. 180240) and BRAF (OMIM Ref. No. 164757), respectively, results in the production of PML-RAR-alpha and TIF1-alpha-B-RAF (T18) oncoproteins. Zhong et al. (1999) showed that PML, TIF1-alpha, and RXR-alpha (OMIM Ref. No. 180245)/RAR-alpha function together in a retinoic acid-dependent transcription complex. Zhong et al. (1999) found that PML acts as a ligand-dependent coactivator of RXR-alpha/RARA-alpha. PML interacts with TIF1-alpha and CREB-binding protein (CBP; 600140). In PML -/- cells, the retinoic acid-dependent induction of genes such as RARB2 and the ability of TIF1-alpha and CBP to act as transcriptional coactivators on retinoic acid are impaired. Zhong et al. (1999) showed that both PML and TIF1-alpha are growth suppressors required for the growth-inhibitory activity of retinoic acid. T18, similar to PML-RAR-alpha, disrupts the retinoic acid-dependent activity of this complex in a dominant-negative manner, resulting in a growth advantage.

PML-RAR-alpha was the first example of an oncoprotein generated by the fusion of 2 molecules participating in the same pathway, specifically the fusion of a transcription factor to one of its own cofactors. Since the PML and RAR-alpha pathways converge at the transcriptional level, there is no need for a double-dominant-negative product to explain the pathogenesis of acute promyelocytic leukemia, or APL. Beckstead et al. (2001) found that the *Drosophila* 'bonus' (bon) gene encodes a homolog of the vertebrate TIF1 transcriptional cofactors. Bon is required for male viability, molting, and numerous events in metamorphosis, including leg elongation, bristle development, and pigmentation. Most of these processes are associated with genes that are implicated in the ecdysone pathway, a nuclear hormone receptor pathway required throughout *Drosophila* development. Bon is associated with sites on the polytene chromosomes and can interact with numerous *Drosophila* nuclear receptor proteins. In vivo, bon behaves as a transcriptional inhibitor.

[9255] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9256] Zhong, S.; Delva, L.; Rachez, C.; Cenciarelli, C.; Gandini,

D.; Zhang, H.; Kalantry, S.; Freedman, L. P.; Pandolfi, P. P. : A RA-dependent, tumour-growth suppressive transcription complex is the target of the PML-RAR-alpha and T18 oncoproteins. *Nature Genet.* 23: 287-295, 1999. ; and

[9257] Beckstead, R.; Ortiz, J. A.; Sanchez, C.; Prokopenko, S. N.; Chambon, P.; Losson, R.; Bellen, H. J. : Bonus, a *Drosophila* homolog of TIF1 proteins, interacts with nuclear receptors and.

[9258] Further studies establishing the function and utilities of TIF1 are found in John Hopkins OMIM database record ID 603406, and in cited publications numbered 5297, 5298-5299, 620 and 11302 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ14855 (Accession NM_033210) is another VGAM108 host target gene. FLJ14855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14855 BINDING SITE, designated SEQ ID:27058, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9259] Another function of VGAM108 is therefore inhibition of FLJ14855 (Accession NM_033210). Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14855. FLJ23462 (Accession NM_024843) is another VGAM108 host target gene. FLJ23462 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23462 BINDING SITE, designated SEQ ID:24263, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9260] Another function of VGAM108 is therefore inhibition of FLJ23462 (Accession NM_024843). Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23462. Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130) is another VGAM108 host target gene. GOLPH3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GOLPH3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLPH3 BINDING SITE, designated SEQ ID:22685, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9261] Another function of VGAM108 is therefore inhibition of Golgi Phosphoprotein 3 (coat-protein) (GOLPH3, Accession NM_022130). Accordingly, utilities of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLPH3. LOC145368 (Accession XM_085112) is another VGAM108 host target gene. LOC145368 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145368 BINDING SITE, designated SEQ ID:37826, to the nucleotide sequence of VGAM108 RNA, herein designated VGAM RNA, also designated SEQ ID:2819.

[9262] Another function of VGAM108 is therefore inhibition of LOC145368 (Accession XM_085112). Accordingly, utilities

of VGAM108 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145368. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 109 (VGAM109) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9263] VGAM109 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM109 was detected is described hereinabove with reference to Figs. 1–8.

[9264] VGAM109 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9265] VGAM109 gene encodes a VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM109 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM109 precursor RNA is designated SEQ ID:95, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:95 is located at position 52022 relative to the genome of Saimiriine Herpesvirus 2.

[9266] VGAM109 precursor RNA folds onto itself, forming VGAM109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9267] An enzyme complex designated DICER COMPLEX, `dices` the VGAM109 folded precursor RNA into VGAM109 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide sequence of VGAM109 RNA is designated SEQ ID:2820, and

is provided hereinbelow with reference to the sequence listing part.

[9268] VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM109 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9269] VGAM109 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM109 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM109 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9270] The complementary binding of VGAM109 RNA, herein designated VGAM RNA, to host target binding sites on VGAM109 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM109 host target RNA into VGAM109 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9271] It is appreciated that VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM109 host target genes. The mRNA of each one of this plurality of VGAM109 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM109 RNA, herein designated VGAM RNA, and which when bound by VGAM109 RNA causes inhibition of translation of respective one or more VGAM109 host target proteins.

[9272] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM109 gene, herein designated VGAM GENE, on one or more VGAM109 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9273] It is yet further appreciated that a function of VGAM109 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM109 correlate with, and may be deduced from, the identity of the host target genes which VGAM109 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9274] Nucleotide sequences of the VGAM109 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM109 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM109 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM109 are further described hereinbelow with reference to Table 1.

[9275] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM109 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM109 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9276] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM109 gene, herein designated VGAM is inhibition of expression of VGAM109 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM109 correlate with, and may be deduced from, the identity of the target genes which VGAM109 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9277] DKFZp547I094 (Accession NM_032155) is a VGAM109 host target gene. DKFZp547I094 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547I094, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I094 BINDING SITE, designated SEQ ID:25858, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9278] A function of VGAM109 is therefore inhibition of DKFZp547I094 (Accession NM_032155). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I094. FLJ11996 (Accession NM_024976) is another VGAM109 host target gene. FLJ11996 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ11996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11996 BINDING SITE, designated SEQ ID:24532, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9279] Another function of VGAM109 is therefore inhibition of FLJ11996 (Accession NM_024976). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11996. FLJ32334 (Accession NM_144565) is another VGAM109 host target gene. FLJ32334 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ32334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32334 BINDING SITE, designated SEQ ID:29366, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9280] Another function of VGAM109 is therefore inhibition of

FLJ32334 (Accession NM_144565). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32334. HBP1 (Accession NM_012257) is another VGAM109 host target gene. HBP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HBP1 BINDING SITE, designated SEQ ID:14561, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9281] Another function of VGAM109 is therefore inhibition of HBP1 (Accession NM_012257). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HBP1. KIAA0063 (Accession NM_014876) is another VGAM109 host target gene. KIAA0063 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0063 BINDING SITE, designated SEQ ID:17018, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9282] Another function of VGAM109 is therefore inhibition of KIAA0063 (Accession NM_014876). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0063. LOC221296 (Accession XM_166325) is another VGAM109 host target gene. LOC221296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221296 BINDING SITE, designated SEQ ID:44172, to the nucleotide sequence of VGAM109 RNA, herein designated VGAM RNA, also designated SEQ ID:2820.

[9283] Another function of VGAM109 is therefore inhibition of LOC221296 (Accession XM_166325). Accordingly, utilities of VGAM109 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221296. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 110 (VGAM110) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9284] VGAM110 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM110 was detected is described hereinabove with reference to Figs. 1–8.

[9285] VGAM110 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9286] VGAM110 gene encodes a VGAM110 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM110 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM110 precursor RNA is designated SEQ ID:96, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:96 is

located at position 161841 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9287] VGAM110 precursor RNA folds onto itself, forming VGAM110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9288] An enzyme complex designated DICER COMPLEX, `dices` the VGAM110 folded precursor RNA into VGAM110 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM110 RNA is designated SEQ ID:2821, and is provided hereinbelow with reference to the sequence listing part.

[9289] VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM110 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9290] VGAM110 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM110 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM110 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9291] The complementary binding of VGAM110 RNA, herein designated VGAM RNA, to host target binding sites on VGAM110 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM110 host target RNA into VGAM110 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9292] It is appreciated that VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM110 host target genes. The mRNA of each one of this plurality of VGAM110 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM110 RNA, herein designated VGAM RNA, and which when bound by VGAM110 RNA causes in-

hibition of translation of respective one or more VGAM110 host target proteins.

[9293] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM110 gene, herein designated VGAM GENE, on one or more VGAM110 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9294] It is yet further appreciated that a function of VGAM110 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM110 include diagnosis, prevention and

treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM110 correlate with, and may be deduced from, the identity of the host target genes which VGAM110 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9295] Nucleotide sequences of the VGAM110 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM110 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM110 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM110 are further described hereinbelow with reference to Table 1.

[9296] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM110 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM110 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9297] As mentioned hereinabove with reference to Fig. 1, a function of VGAM110 gene, herein designated VGAM is

inhibition of expression of VGAM110 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM110 correlate with, and may be deduced from, the identity of the target genes which VGAM110 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9298] Dual Specificity Phosphatase 4 (DUSP4, Accession NM_001394) is a VGAM110 host target gene. DUSP4 BINDING SITE1 and DUSP4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DUSP4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP4 BINDING SITE1 and DUSP4 BINDING SITE2, designated SEQ ID:7089 and SEQ ID:27664 respectively, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9299] A function of VGAM110 is therefore inhibition of Dual Specificity Phosphatase 4 (DUSP4, Accession NM_001394), a gene which regulates mitogenic signal transduction. Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with DUSP4. The function of DUSP4 has been established by previous studies. The VH1 phosphatase encoded by the vaccinia virus is a dual-specificity protein phosphatase that can dephosphorylate both serine/threonine and tyrosine residues. Cellular proteins homologous to VH1 are thought to regulate mitogen-activated protein (MAP) kinases. By screening a placenta library with a DUSP1 (OMIM Ref. No. 600714) cDNA, Guan and Butch (1995) identified cDNAs encoding DUSP4, which they called HVH2. Northern blot analysis revealed that DUSP4 is expressed as 2.5- and 6-kb mRNAs in placenta and, at lower levels, in pancreas. The sequence of the predicted 394-amino acid DUSP4 protein was 62% and 55% identical to those of DUSP1 and PAC1, respectively. Like DUSP1 and DUSP6 (OMIM Ref. No. 602748), the N-terminal region of DUSP4 shares significant identity with CDC25 (OMIM Ref. No. 157680). By immunofluorescence of mammalian cells expressing epitope-tagged protein, Guan and Butch (1995) found that DUSP4 was localized within the nucleus. Purified recombinant DUSP4 specifically hydrolyzed the phosphothreonine and phosphotyrosine residues of the activated MAP kinases ERK1 (OMIM Ref. No. 601795) and ERK2 (OMIM Ref. No. 176948). Expression of DUSP4 in

mammalian cells blocked activation of a MAP kinase-regulated reporter gene. These results led Guan and Butch (1995) to suggest that DUSP4 plays a role in the MAP kinase signal transduction pathway. By fluorescence in situ hybridization, Smith et al. (1997) mapped the DUSP4 gene to 8p12-p11.

[9300] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9301] Guan, K.-L.; Butch, E. : Isolation and characterization of a novel dual specific phosphatase, HVH2, which selectively dephosphorylates the mitogen-activated protein kinase. J. Biol. Chem. 270: 7197-7203, 1995. ; and

[9302] Smith, A.; Price, C.; Cullen, M.; Muda, M.; King, A.; Ozanne, B.; Arkinstall, S.; Ashworth, A. : Chromosomal localization of three human dual specificity phosphatase genes (DUSP4, DUSP6.

[9303] Further studies establishing the function and utilities of DUSP4 are found in John Hopkins OMIM database record ID 602747, and in cited publications numbered 2408-2409 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibroblast Growth Factor 13 (FGF13, Accession

NM_033642) is another VGAM110 host target gene.

FGF13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF13 BINDING SITE, designated SEQ ID:27361, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9304] Another function of VGAM110 is therefore inhibition of Fibroblast Growth Factor 13 (FGF13, Accession NM_033642), a gene which probably involved in nervous system development and function. Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF13. The function of FGF13 has been established by previous studies. See fibroblast growth factor-12 (FGF12; 601513). By Southern blot hybridization of genomic DNA from rodent/human hybrid cell lines carrying individual human chromosomes, Smallwood et al. (1996) mapped the FGF2 gene (also symbolized FGF13) to the X chromosome. By using an interspecific backcross mapping panel, they

demonstrated that the mouse gene, Fhf2, shows no recombination with the gene for CD40 antigen ligand (OMIM Ref. No. 300386). Thus the human gene is probably located at Xq26. By use of isotopic in situ hybridization, Lovec et al. (1997) assigned the FHF2 gene to Xq21. Gecz et al. (1999), however, provided evidence that the FHF2 gene is located in Xq26.3. They identified a male patient with features of Borjeson–Forssman–Lehmann syndrome (BFLS; 301900) and a duplication of the Xq26–q28 region. By FISH using YAC clones from Xq26, they localized the duplication breakpoint to an interval of approximately 400 kb in the Xq26.3 region between DXS155 and DXS294/DXS730. Database searches and an analysis of available genomic sequence from the region showed that the FHF2 gene is located within the duplication breakpoint interval. Gecz et al. (1999) determined the structure of the FHF2 gene and identified 2 new exons, including a new 5–prime end exon, designated 1B. FHF2 is a large gene, extending over approximately 200 kb in Xq26.3, and contains at least 7 exons. It shows tissue–specific alternative splicing and alternative transcription starts. Northern blot hybridization showed highest expression in brain and skeletal muscle. The localization and tissue–specific ex–

pression pattern of FHF2 made it a possible candidate gene for familial cases of BFLS and for other syndromal and nonspecific forms of X-linked mental retardation mapping to that region.

[9305] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9306] Gecz, J.; Baker, E.; Donnelly, A.; Ming, J. E.; McDonald-McGinn, D. M.; Spinner, N. B.; Zackai, E. H.; Sutherland, G. R.; Mulley, J. C. : Fibroblast growth factor homologous factor 2 (FHF2): gene structure, expression and mapping to the Borjeson-Forssman-Lehmann syndrome region in Xq26 delineated by a duplication breakpoint in a BFLS-like patient. Hum. Genet. 104: 56-63, 1999. ; and

[9307] Lovec, H.; Hartung, H.; Verdier, A.-S.; Mattei, M.-G.; Birnbaum, D.; Goldfarb, M.; Coulier, F. : Assignment of FGF13 to human chromosome band Xq21 by in situ hybridization. Cytogenet.

[9308] Further studies establishing the function and utilities of FGF13 are found in John Hopkins OMIM database record ID 300070, and in cited publications numbered 9084-9086 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. IQ Motif

Containing GTPase Activating Protein 2 (IQGAP2, Accession NM_006633) is another VGAM110 host target gene. IQGAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IQGAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IQGAP2 BINDING SITE, designated SEQ ID:13427, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9309] Another function of VGAM110 is therefore inhibition of IQ Motif Containing GTPase Activating Protein 2 (IQGAP2, Accession NM_006633), a gene which Inhibits GTPase activity of Cdc42 and Rac1. Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IQGAP2. The function of IQGAP2 has been established by previous studies. Sugimoto et al. (2001) demonstrated that IQGAP1, a negative regulator of cell-cell adhesion, is upregulated by gene amplification at 15q26 in 2 gastric cancer cell lines. Amplification at 15q26 had been found in various malignancies, including breast cancers, and FES (OMIM Ref. No.

190030) and/or IGF1R (OMIM Ref. No. 147370) had been identified as targets for gene amplification in breast cancer, melanoma, and pancreatic adenocarcinoma. In contrast, Sugimoto et al. (2001) found that both genes are located telomeric to the amplicon at 15q26 in the 2 gastric cancer cell lines they studied. Fukata et al. (2002) found that IQGAP1, an effector of RAC1 (OMIM Ref. No. 602048) and CDC42, interacts with CLIP170 (RSN; 179838). In Vero fibroblasts, IQGAP1 localized at the polarized leading edge. Expression of a C-terminal fragment of IQGAP1 that included the CLIP170-binding region delocalized GFP-CLIP170 from the tips of microtubules and altered the microtubule array. The authors found that activated RAC1/CDC42, IQGAP1, and CLIP170 form a tripartite complex. Furthermore, expression of an IQGAP1 mutant defective in RAC1/CDC42 binding induced multiple leading edges. These results indicated that RAC1/CDC42 marks special cortical spots where the IQGAP1 and CLIP170 complex is targeted, leading to a polarized microtubule array and cell polarization.

[9310] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9311] Sugimoto, N.; Imoto, I.; Fukuda, Y.; Kurihara, N.; Kuroda, S.; Tanigami, A.; Kaibuchi, K.; Kamiyama, R.; Inazawa, J. : IQGAP1, a negative regulator of cell–cell adhesion, is up-regulated by gene amplification at 15q26 in gastric cancer cell lines HSC39 and 40A. J. Hum. Genet. 46: 21–25, 2001. ; and

[9312] Fukata, M.; Watanabe, T.; Noritake, J.; Nakagawa, M.; Yamaga, M.; Kuroda, S.; Matsuura, Y.; Iwamatsu, A.; Perez, F.; Kaibuchi, K. : Rac1 and Cdc42 capture microtubules through IQGAP1 an.

[9313] Further studies establishing the function and utilities of IQGAP2 are found in John Hopkins OMIM database record ID 605401, and in cited publications numbered 7315 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin–1 Receptor–associated Kinase 1 (IRAK1, Accession NM_001569) is another VGAM110 host target gene. IRAK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IRAK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRAK1 BINDING SITE, designated SEQ ID:7297, to the nu–

cleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9314] Another function of VGAM110 is therefore inhibition of Interleukin-1 Receptor-associated Kinase 1 (IRAK1, Accession NM_001569). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRAK1. Kelch-like 2, Mayven (Drosophila) (KLHL2, Accession NM_007246) is another VGAM110 host target gene. KLHL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL2 BINDING SITE, designated SEQ ID:14111, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9315] Another function of VGAM110 is therefore inhibition of Kelch-like 2, Mayven (Drosophila) (KLHL2, Accession NM_007246). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL2. Oligophrenin 1 (OPHN1, Accession NM_002547) is another VGAM110 host

target gene. OPHN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8399, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9316] Another function of VGAM110 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM_002547). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPHN1. Williams-Beuren Syndrome Chromosome Region 1 (WBSCR1, Accession NM_022170) is another VGAM110 host target gene. WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WBSCR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2, designated SEQ ID:22725 and SEQ ID:25708

respectively, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9317] Another function of VGAM110 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 1 (WBSCR1, Accession NM_022170), a gene which stimulates protein translation. Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR1. The function of WBSCR1 has been established by previous studies. Williams–Beuren syndrome (WBS; 194050) is a multisystem developmental disorder caused by the deletion of contiguous genes at 7q11.23. Osborne et al. (1996) characterized a 500–kb region in 7q11.23 that was deleted in a collection of 30 WBS patients. They constructed a detailed physical map of the region consisting of cosmids, P1 artificial chromosomes, and yeast artificial chromosomes. They identified 9 transcription units from the area, including the previously characterized genes ELN (OMIM Ref. No. 130160), LIMK1 (OMIM Ref. No. 601329), and RFC2 (OMIM Ref. No. 600404), and the novel genes WSCR1 and WSCR4 (OMIM Ref. No. 603432). The WSCR1 gene has 6 exons which contain an open reading frame

encoding 232 amino acids, including an RNA-binding domain consensus sequence. Northern blot analysis detected a 2.5-kb WBSCR1 transcript in all human cell lines analyzed. Richter-Cook et al. (1998) identified the eukaryotic initiation factor (EIF) 4H protein from rabbit reticulocyte lysate on the basis of its ability to stimulate translation in an in vitro globin synthesis assay deficient in EIF4B (OMIM Ref. No. 603928) and EIF4F. Amino acid sequence analysis of 3 EIF4H tryptic fragments revealed 100% sequence identity to the human WBSCR1 protein. The authors demonstrated that the 25-kD rabbit EIF4H protein stimulates the in vitro activities of EIF4B and EIF4F in globin synthesis, as well as the in vitro RNA-dependent ATPase activities of EIF4A (e.g., 601102), EIF4B, and EIF4F.

[9318] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9319] Osborne, L. R.; Martindale, D.; Scherer, S. W.; Shi, X.-M.; Huizenga, J.; Heng, H. H. Q.; Costa, T.; Pober, B.; Lew, L.; Brinkman, J.; Rommens, J.; Koop, B.; Tsui, L.-C. : Identification of genes from a 500-kb region at 7q11.23 that is commonly deleted in Williams syndrome patients. *Genomics* 36: 328-336, 1996. ; and

[9320] Richter–Cook, N. J.; Dever, T. E.; Hensold, J. O.; Merrick, W. C. : Purification and characterization of a new eukaryotic protein translation factor: eukaryotic initiation factor 4H. J.

[9321] Further studies establishing the function and utilities of WBSCR1 are found in John Hopkins OMIM database record ID 603431, and in cited publications numbered 10456 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.UDP–GlcNAc:betaGal Beta–1,3–N–acetylglucosaminyltransferase 5 (B3GNT5, Accession NM_032047) is another VGAM110 host target gene. B3GNT5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by B3GNT5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT5 BINDING SITE, designated SEQ ID:25763, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9322] Another function of VGAM110 is therefore inhibition of UDP–GlcNAc:betaGal Beta–

1,3-N-acetylglucosaminyltransferase 5 (B3GNT5, Accession NM_032047). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT5. FEM-2 (Accession NM_014634) is another VGAM110 host target gene. FEM-2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FEM-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FEM-2 BINDING SITE, designated SEQ ID:16005, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9323] Another function of VGAM110 is therefore inhibition of FEM-2 (Accession NM_014634). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FEM-2. FLJ11259 (Accession NM_018370) is another VGAM110 host target gene. FLJ11259 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11259 BINDING SITE, designated SEQ ID:20380, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9324] Another function of VGAM110 is therefore inhibition of FLJ11259 (Accession NM_018370). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11259. FLJ14437 (Accession NM_032578) is another VGAM110 host target gene. FLJ14437 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14437 BINDING SITE, designated SEQ ID:26305, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9325] Another function of VGAM110 is therefore inhibition of FLJ14437 (Accession NM_032578). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14437.

KIAA0459 (Accession XM_027862) is another VGAM110 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30570, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9326] Another function of VGAM110 is therefore inhibition of KIAA0459 (Accession XM_027862). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0459. KIAA0547 (Accession NM_014793) is another VGAM110 host target gene. KIAA0547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0547 BINDING SITE, designated SEQ ID:16697, to the nucleotide sequence of VGAM110 RNA, herein designated

VGAM RNA, also designated SEQ ID:2821.

[9327] Another function of VGAM110 is therefore inhibition of KIAA0547 (Accession NM_014793). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0547. KIAA1762 (Accession XM_033370) is another VGAM110 host target gene. KIAA1762 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1762, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1762 BINDING SITE, designated SEQ ID:31908, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9328] Another function of VGAM110 is therefore inhibition of KIAA1762 (Accession XM_033370). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1762. KIAA1951 (Accession XM_057401) is another VGAM110 host target gene. KIAA1951 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1951, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1951 BINDING SITE, designated SEQ ID:36511, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9329] Another function of VGAM110 is therefore inhibition of KIAA1951 (Accession XM_057401). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1951. LOC145900 (Accession XM_085276) is another VGAM110 host target gene. LOC145900 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145900 BINDING SITE, designated SEQ ID:38010, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9330] Another function of VGAM110 is therefore inhibition of LOC145900 (Accession XM_085276). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC145900. LOC150933 (Accession XM_097971) is another VGAM110 host target gene. LOC150933 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150933, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150933 BINDING SITE, designated SEQ ID:41269, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9331] Another function of VGAM110 is therefore inhibition of LOC150933 (Accession XM_097971). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150933. LOC152876 (Accession XM_098279) is another VGAM110 host target gene. LOC152876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152876 BINDING SITE, designated SEQ ID:41559, to

the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9332] Another function of VGAM110 is therefore inhibition of LOC152876 (Accession XM_098279). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152876. LOC254936 (Accession XM_170770) is another VGAM110 host target gene. LOC254936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254936 BINDING SITE, designated SEQ ID:45525, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9333] Another function of VGAM110 is therefore inhibition of LOC254936 (Accession XM_170770). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254936. LOC256867 (Accession XM_170694) is another VGAM110 host target gene. LOC256867 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC256867, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256867 BINDING SITE, designated SEQ ID:45469, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9334] Another function of VGAM110 is therefore inhibition of LOC256867 (Accession XM_170694). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256867. LOC90190 (Accession XM_029758) is another VGAM110 host target gene. LOC90190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90190 BINDING SITE, designated SEQ ID:30944, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9335] Another function of VGAM110 is therefore inhibition of LOC90190 (Accession XM_029758). Accordingly, utilities

of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90190. LOC90639 (Accession XM_033092) is another VGAM110 host target gene. LOC90639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90639 BINDING SITE, designated SEQ ID:31831, to the nucleotide sequence of VGAM110 RNA, herein designated VGAM RNA, also designated SEQ ID:2821.

[9336] Another function of VGAM110 is therefore inhibition of LOC90639 (Accession XM_033092). Accordingly, utilities of VGAM110 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90639. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 111 (VGAM111) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9337] VGAM111 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM111 was detected is described hereinabove with reference to Figs. 1–8.

[9338] VGAM111 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9339] VGAM111 gene encodes a VGAM111 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM111 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM111 precursor RNA is designated SEQ ID:97, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:97 is located at position 193387 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9340] VGAM111 precursor RNA folds onto itself, forming VGAM111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[9341] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM111 folded precursor RNA into VGAM111 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM111 RNA is designated SEQ ID:2822, and
is provided hereinbelow with reference to the sequence
listing part.

[9342] VGAM111 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM111 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM111 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[9343] VGAM111 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM111 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM111 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[9344] The complementary binding of VGAM111 RNA, herein designated VGAM RNA, to host target binding sites on VGAM111 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM111 host target RNA into VGAM111 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9345] It is appreciated that VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM111 host target genes. The mRNA of each one of this plurality of VGAM111 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM111 RNA, herein designated VGAM RNA, and which when bound by VGAM111 RNA causes inhibition of translation of respective one or more VGAM111 host target proteins.

[9346] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM111 gene, herein designated VGAM GENE, on one or

more VGAM111 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9347] It is yet further appreciated that a function of VGAM111 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM111 correlate with, and may be deduced from, the identity of the host target genes which VGAM111 binds and inhibits, and the function of these host target genes, as elaborated herein-

below.

- [9348] Nucleotide sequences of the VGAM111 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM111 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM111 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM111 are further described hereinbelow with reference to Table 1.
- [9349] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM111 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM111 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [9350] As mentioned hereinabove with reference to Fig. 1, a function of VGAM111 gene, herein designated VGAM is inhibition of expression of VGAM111 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM111 correlate with, and may be deduced from, the identity of the target genes which VGAM111 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9351] Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834) is a VGAM111 host target gene. GRIN2B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GRIN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2B BINDING SITE, designated SEQ ID:6492, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9352] A function of VGAM111 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2B (GRIN2B, Accession NM_000834). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN2B. Potassium Large Conductance Calcium-activated Channel, Subfamily M Beta Member 3 (KCNMB3, Accession NM_014407) is another VGAM111 host target gene. KCNMB3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KCNMB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of KCNMB3 BINDING SITE, designated SEQ ID:15748, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9353] Another function of VGAM111 is therefore inhibition of Potassium Large Conductance Calcium-activated Channel, Subfamily M Beta Member 3 (KCNMB3, Accession NM_014407), a gene which is similar to a regulatory subunit of Ca-activated potassium channel. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNMB3. The function of KCNMB3 has been established by previous studies. The large conductance, calcium-activated potassium (BK) channel is a member of the Shaker-related 6-transmembrane domain potassium channel superfamily that is sensitive to voltage and calcium. BK channels are composed of a pore-forming alpha subunit (KCNMA1, or HSLO; 600150) and, in some tissues, a beta subunit. The beta-1 subunit (KCNMB1; 603951) is expressed predominantly in smooth muscle cells, whereas the beta-2 subunit (KCNMB2; 605214) is expressed in endocrine tissue, such as adrenal chromaffin cells Uebele et

al. (2000) determined that KCNMB3 is a family of 4 related subunits, KCNMB3a (277 amino acids), KCNMB3b (257 amino acids), KCNMB3c (275 amino acids), and KCNMB3d (279 amino acids), that arise from alternative splicing. The subunits vary only in their cytoplasmic N-terminal sequences and share 256 C-terminal amino acids. Genomic sequence analysis determined that the KCNMB3 gene contains 6 exons, 3 of which (1a, 1b, and 1c/d) encode sequences unique to each of the splice variants. RT-PCR analysis showed that KCNMB3a has a relatively restricted distribution (spleen, placenta, pancreas, kidney, and heart), while the other variants are more widely expressed. KCNMB3c was notably abundant in pancreas. In situ hybridization analysis demonstrated that KCNMB3c expression is restricted to pancreatic beta cells. Coexpression of KCNMB3a, -b, and -c with KCNMA1 resulted in partial inactivation of activating currents; KCNMB3d did not induce detectable inactivation. By FISH and somatic cell hybrid analysis, Riazi et al. (1999) mapped the KCNMB3 gene to 3q26.3-q27. Uebele et al. (2000) also mapped the KCNMB3 gene to 3q26.3-q27.1, in close proximity to KCNMB2, by radiation hybrid and FISH analysis

- [9354] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9355] Behrens, R.; Nolting, A.; Reimann, F.; Schwarz, M.; Waldschütz, R.; Pongs, O. : hKCNMB3 and hKCNMB4, cloning and characterization of two members of the large-conductance calcium-activated potassium channel beta subunit family. FEBS Lett. 474: 99–106, 2000. ; and
- [9356] Brenner, R.; Jegla, T. J.; Wickenden, A.; Liu, Y.; Aldrich, R. W. : Cloning and functional characterization of novel large conductance calcium-activated potassium channel beta subunits.
- [9357] Further studies establishing the function and utilities of KCNMB3 are found in John Hopkins OMIM database record ID 605222, and in cited publications numbered 6974–697 and 6965 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Membrane-spanning 4-domains, Subfamily A, Member 3 (hematopoietic cell-specific) (MS4A3, Accession NM_006138) is another VGAM111 host target gene. MS4A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MS4A3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MS4A3 BINDING SITE, designated SEQ ID:12779, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9358] Another function of VGAM111 is therefore inhibition of Membrane-spanning 4-domains, Subfamily A, Member 3 (hematopoietic cell-specific) (MS4A3, Accession NM_006138). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MS4A3. Neuronal Pentraxin I (NPTX1, Accession NM_002522) is another VGAM111 host target gene. NPTX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPTX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPTX1 BINDING SITE, designated SEQ ID:8353, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9359] Another function of VGAM111 is therefore inhibition of

Neuronal Pentraxin I (NPTX1, Accession NM_002522), a gene which may be involved in synaptic uptake of extracellular material and is very strongly similar to rat NP1. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTX1. The function of NPTX1 has been established by previous studies. See 600750. Neuronal pentraxin I (NP1) was identified in the rat as a binding protein for the snake venom toxin taipoxin (Schlimgen et al., 1995). Omeis et al. (1996) cloned the human NP1 homolog by screening a human cerebellar cDNA library with the rat NP1 gene as a probe. The gene, designated NPTX1, encodes a predicted 430-amino acid protein that is 95% identical to rat NP1. Northern blot analysis showed that the approximately 6-kb NPTX1 mRNA is expressed only in the brain. Omeis et al. (1996) used fluorescence in situ hybridization to map the NPTX1 gene to human chromosome 17q25.1-q25.2 and mouse chromosome 11e2-e1.3.

[9360] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9361] Omeis, I. A.; Hsu, Y.-C.; Perin, M. S. : Mouse and human

neuronal pentraxin 1 (NPXT1): conservation, genomic structure, and chromosomal localization. Genomics 36: 543–545, 1996. ; and

[9362] Schlimgen, A. K.; Helms, J. A.; Vogel, H.; Perin, M. S. : Neuronal pentraxin, a secreted protein with homology to acute phase proteins of the immune system. Neuron 14: 519–526, 1995.

[9363] Further studies establishing the function and utilities of NPTX1 are found in John Hopkins OMIM database record ID 602367, and in cited publications numbered 8933 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198) is another VGAM111 host target gene. PDK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK4 BINDING SITE, designated SEQ ID:46441, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9364] Another function of VGAM111 is therefore inhibition of

Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK4. Selectin P (granule membrane protein 140kDa, antigen CD62) (SELP, Accession NM_003005) is another VGAM111 host target gene. SELP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SELP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SELP BINDING SITE, designated SEQ ID:8913, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9365] Another function of VGAM111 is therefore inhibition of Selectin P (granule membrane protein 140kDa, antigen CD62) (SELP, Accession NM_003005), a gene which mediates the interaction of activated endothelial cells or platelets with leukocytes. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELP. The function of SELP has been established by previous studies. P-selectin, also called GMP-140, CD62, or selectin P, is a

140-kD adhesion molecule, expressed at the surface of activated cells, that mediates the interaction of activated endothelial cells or platelets with leukocytes. McEver et al. (1989) used an immunoperoxidase procedure to examine the distribution of GMP-140 in human tissues. The protein was detected in megakaryocytes and platelets, as well as in vascular endothelial cells, but was not found in a variety of other cell types examined. In endothelial cells, the protein was localized to the membranes of Weibel-Palade bodies, the intracellular storage granules for von Willebrand factor. The gene for GMP-140 was cloned by Johnston et al. (1989). Johnston et al. (1990) found that the GMP140 gene spans over 50 kb and contains 17 exons. CD24 is a ligand for P-selectin; see 600074. Animal model experiments lend further support to the function of SELP. Mayadas et al. (1993) generated P-selectin-deficient mice by gene targeting in embryonic stem cells and found that they exhibited a number of defects in leukocyte behavior, including elevated numbers of circulating neutrophils, virtually total absence of leukocyte rolling in mesenteric venules, and delayed recruitment of neutrophils to the peritoneal cavity upon experimentally induced inflammation.

[9366] It is appreciated that the abovementioned animal model for SELP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9367] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9368] McEver, R. P.; Beckstead, J. H.; Moore, K. L.; Marshall-Carlson, L.; Bainton, D. F. : GMP-140, a platelet alpha-granule membrane protein, is also synthesized by vascular endothelial cells and is localized in Weibel-Palade bodies. J. Clin. Invest. 84: 92-99, 1989. ; and

[9369] Herrmann, S.-M.; Ricard, S.; Nicaud, V.; Mallet, C.; Evans, A.; Ruidavets, J.-B.; Arveiler, D.; Luc, G.; Cambien, F. : The P-selectin gene is highly polymorphic: reduced frequency of the.

[9370] Further studies establishing the function and utilities of SELP are found in John Hopkins OMIM database record ID 173610, and in cited publications numbered 11805-1710, 2123, 1150 and 11810 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM_049695) is another VGAM111

host target gene. VANGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VANGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VANGL2 BINDING SITE, designated SEQ ID:35481, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9371] Another function of VGAM111 is therefore inhibition of Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM_049695), a gene which may take part in defining the lateral boundary of floorplate differentiation. Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VANGL2. The function of VANGL2 has been established by previous studies. Murdoch et al. (2001) independently cloned the causative gene for craniorachischisis in Lp mice, which they named Lpp1. A single base transition, 1841G→A, resulted in a ser464→asn substitution. Lpp1 is expressed in the ventral part of the developing neural tube, but is excluded from the floorplate where Sonic hedgehog (Shh; 600725) is expressed. Embryos

lacking Shh express Lpp1 throughout the ventral neural tube, suggesting negative regulation of Lpp1 by Shh. The authors suggested that the mutual interaction between Lpp1 and Shh may define the lateral boundary of floor-plate differentiation. They hypothesized that loss of Lpp1 function may disrupt neurulation by permitting more extensive floorplate induction by Shh, thereby inhibiting midline bending of the neural plate during initiation of neurulation. The human ortholog of Lpp1, which maps to chromosome 1, shares 89% identity with the mouse gene at the nucleotide level and 99% identity at the amino acid level. Animal model experiments lend further support to the function of VANGL2. 'Loop-tail' (Lp) is a semidominant mouse mutation that, in homozygous mutants, causes a severe form of neural tube defect called craniorachischisis. Heterozygous mice exhibit a characteristic looped tail, and homozygous embryos show a completely open neural tube in the hindbrain and spinal region. Kibar et al. (2001) used a positional cloning approach to identify the Lp gene. By an in silico search, the authors identified a mouse EST within the Lp interval homologous to a partial human cDNA clone KIAA1215. Based on its relationship to the mouse disorder, Kibar et al. (2001) used the tempo-

rary designation 'loop-tail-associated protein' (Ltap). The Ltap gene encodes a homolog of *Drosophila* 'strabismus/Van Gogh' (Stbm/Vang), a component of the frizzled-disheveled tissue polarity pathway. Ltap is expressed broadly in the neuroectoderm throughout early neurogenesis. This and the fact that the gene was altered in 2 independent Lp alleles identified it as the likely basis for loop-tail. The authors suggested that the human Ltap homolog is worthy of search for mutations that may be associated with sporadic or familial cases of neural tube defects in humans.

[9372] It is appreciated that the abovementioned animal model for VANGL2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9373] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9374] Murdoch, J. N.; Doudney, K.; Paternotte, C.; Copp, A. J.; Stanier, P. : Severe neural tube defects in the loop-tail mouse result from mutation of Lpp1, a novel gene involved in floor plate specification. *Hum. Molec. Genet.* 10: 2593–2601, 2001. ; and

- [9375] Kibar, Z.; Vogan, K. J.; Groulx, N.; Justice, M. J.; Underhill, D. A.; Gros, P. : Ltap, a mammalian homolog of Drosophila Strabismus/Van Gogh, is altered in the mouse neural tube mutant lo.
- [9376] Further studies establishing the function and utilities of VANGL2 are found in John Hopkins OMIM database record ID 600533, and in cited publications numbered 7767–7771 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ADMP (Accession NM_145035) is another VGAM111 host target gene. ADMP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADMP BINDING SITE, designated SEQ ID:29656, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.
- [9377] Another function of VGAM111 is therefore inhibition of ADMP (Accession NM_145035). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADMP. V-akt Murine Thymoma Viral Oncogene Homolog 3 (protein

kinase B, gamma) (AKT3, Accession NM_005465) is another VGAM111 host target gene. AKT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT3 BINDING SITE, designated SEQ ID:11958, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9378] Another function of VGAM111 is therefore inhibition of V-akt Murine Thymoma Viral Oncogene Homolog 3 (protein kinase B, gamma) (AKT3, Accession NM_005465). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT3. Aquaporin 9 (AQP9, Accession NM_020980) is another VGAM111 host target gene. AQP9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP9 BINDING SITE, designated SEQ ID:21967, to the nu-

cleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9379] Another function of VGAM111 is therefore inhibition of Aquaporin 9 (AQP9, Accession NM_020980). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP9. ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM111 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31084, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9380] Another function of VGAM111 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605) is another

VGAM111 host target gene. C5orf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C5orf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf6 BINDING SITE, designated SEQ ID:18703, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9381] Another function of VGAM111 is therefore inhibition of Chromosome 5 Open Reading Frame 6 (C5orf6, Accession NM_016605). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf6. FLJ10769 (Accession NM_018210) is another VGAM111 host target gene. FLJ10769 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10769, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10769 BINDING SITE, designated SEQ ID:20114, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ

ID:2822.

[9382] Another function of VGAM111 is therefore inhibition of FLJ10769 (Accession NM_018210). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10769. FLJ12572 (Accession NM_022905) is another VGAM111 host target gene. FLJ12572 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23199, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9383] Another function of VGAM111 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. FLJ14624 (Accession XM_049060) is another VGAM111 host target gene. FLJ14624 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14624, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14624 BINDING SITE, designated SEQ ID:35337, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9384] Another function of VGAM111 is therefore inhibition of FLJ14624 (Accession XM_049060). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14624. Formin Binding Protein 3 (FNBP3, Accession XM_087118) is another VGAM111 host target gene. FNBP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FNBP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FNBP3 BINDING SITE, designated SEQ ID:39073, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9385] Another function of VGAM111 is therefore inhibition of Formin Binding Protein 3 (FNBP3, Accession XM_087118). Accordingly, utilities of VGAM111 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with FNBP3. KIAA0087 (Accession NM_014769) is another VGAM111 host target gene. KIAA0087 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0087, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0087 BINDING SITE, designated SEQ ID:16558, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9386] Another function of VGAM111 is therefore inhibition of KIAA0087 (Accession NM_014769). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0087. KIAA0335 (Accession NM_014803) is another VGAM111 host target gene. KIAA0335 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0335, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0335 BINDING SITE, designated SEQ ID:16727, to the

nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9387] Another function of VGAM111 is therefore inhibition of KIAA0335 (Accession NM_014803). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0335. KIAA1671 (Accession XM_037809) is another VGAM111 host target gene. KIAA1671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1671 BINDING SITE, designated SEQ ID:32693, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9388] Another function of VGAM111 is therefore inhibition of KIAA1671 (Accession XM_037809). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1671. MGC14836 (Accession NM_033412) is another VGAM111 host target gene. MGC14836 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by MGC14836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14836 BINDING SITE, designated SEQ ID:27235, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9389] Another function of VGAM111 is therefore inhibition of MGC14836 (Accession NM_033412). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14836. MGC16385 (Accession NM_145039) is another VGAM111 host target gene. MGC16385 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC16385, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16385 BINDING SITE, designated SEQ ID:29662, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9390] Another function of VGAM111 is therefore inhibition of MGC16385 (Accession NM_145039). Accordingly, utilities

of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16385. MGC20235 (Accession NM_145041) is another VGAM111 host target gene. MGC20235 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC20235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20235 BINDING SITE, designated SEQ ID:29666, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9391] Another function of VGAM111 is therefore inhibition of MGC20235 (Accession NM_145041). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20235. p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168) is another VGAM111 host target gene. PAK6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of PAK6 BINDING SITE, designated SEQ ID:21386, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9392] Another function of VGAM111 is therefore inhibition of p21(CDKN1A)-activated Kinase 6 (PAK6, Accession NM_020168). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK6. PDZ-GEF1 (Accession NM_014247) is another VGAM111 host target gene. PDZ-GEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDZ-GEF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDZ-GEF1 BINDING SITE, designated SEQ ID:15522, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9393] Another function of VGAM111 is therefore inhibition of PDZ-GEF1 (Accession NM_014247). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDZ-GEF1. PRO0641 (Accession NM_014135) is another

VGAM111 host target gene. PRO0641 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO0641, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0641 BINDING SITE, designated SEQ ID:15400, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9394] Another function of VGAM111 is therefore inhibition of PRO0641 (Accession NM_014135). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0641. PRO1430 (Accession NM_018599) is another VGAM111 host target gene. PRO1430 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1430 BINDING SITE, designated SEQ ID:20674, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9395] Another function of VGAM111 is therefore inhibition of PRO1430 (Accession NM_018599). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1430. Regulator of G-protein Signalling 20 (RGS20, Accession NM_003702) is another VGAM111 host target gene. RGS20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS20 BINDING SITE, designated SEQ ID:9802, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9396] Another function of VGAM111 is therefore inhibition of Regulator of G-protein Signalling 20 (RGS20, Accession NM_003702). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS20. SKI-like (SKIL, Accession NM_005414) is another VGAM111 host target gene. SKIL BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SKIL, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIL BINDING SITE, designated SEQ ID:11883, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9397] Another function of VGAM111 is therefore inhibition of SKI-like (SKIL, Accession NM_005414). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIL. Solute Carrier Family 2 (facilitated glucose transporter), Member 10 (SLC2A10, Accession NM_030777) is another VGAM111 host target gene. SLC2A10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A10 BINDING SITE, designated SEQ ID:25063, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9398] Another function of VGAM111 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 10 (SLC2A10, Accession NM_030777). Accord-

ingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A10. LOC149134 (Accession XM_097594) is another VGAM111 host target gene. LOC149134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149134 BINDING SITE, designated SEQ ID:40959, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9399] Another function of VGAM111 is therefore inhibition of LOC149134 (Accession XM_097594). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149134. LOC91549 (Accession XM_039115) is another VGAM111 host target gene. LOC91549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC91549 BINDING SITE, designated SEQ ID:33013, to the nucleotide sequence of VGAM111 RNA, herein designated VGAM RNA, also designated SEQ ID:2822.

[9400] Another function of VGAM111 is therefore inhibition of LOC91549 (Accession XM_039115). Accordingly, utilities of VGAM111 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91549. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 112 (VGAM112) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9401] VGAM112 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM112 was detected is described hereinabove with reference to Figs. 1–8.

[9402] VGAM112 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9403] VGAM112 gene encodes a VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM112 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM112 precursor RNA is designated SEQ ID:98, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:98 is located at position 52615 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9404] VGAM112 precursor RNA folds onto itself, forming VGAM112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9405] An enzyme complex designated DICER COMPLEX, `dices` the VGAM112 folded precursor RNA into VGAM112 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM112 RNA is designated SEQ ID:2823, and is provided hereinbelow with reference to the sequence listing part.

[9406] VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM112 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9407] VGAM112 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM112 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM112 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9408] The complementary binding of VGAM112 RNA, herein designated VGAM RNA, to host target binding sites on VGAM112 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM112 host target RNA into VGAM112 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9409] It is appreciated that VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM112 host target genes. The mRNA of each one of this plurality of VGAM112 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM112 RNA, herein designated VGAM RNA, and which when bound by VGAM112 RNA causes inhibition of translation of respective one or more VGAM112 host target proteins.

[9410] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM112 gene, herein designated VGAM GENE, on one or more VGAM112 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9411] It is yet further appreciated that a function of VGAM112 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM112 correlate with, and may be deduced from, the identity of the host target genes which VGAM112 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9412] Nucleotide sequences of the VGAM112 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM112 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM112 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM112 are further described hereinbelow with reference to Table 1.

[9413] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM112 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM112 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9414] As mentioned hereinabove with reference to Fig. 1, a function of VGAM112 gene, herein designated VGAM is inhibition of expression of VGAM112 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM112 correlate with, and may be deduced from, the identity of the target genes which VGAM112 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9415] Homeo Box A3 (HOXA3, Accession NM_030661) is a VGAM112 host target gene. HOXA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXA3 BINDING SITE, designated SEQ ID:24992, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA,

also designated SEQ ID:2823.

[9416] A function of VGAM112 is therefore inhibition of Homeo Box A3 (HOXA3, Accession NM_030661). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXA3. Peripheral Myelin Protein 22 (PMP22, Accession NM_000304) is another VGAM112 host target gene. PMP22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMP22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMP22 BINDING SITE, designated SEQ ID:5846, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9417] Another function of VGAM112 is therefore inhibition of Peripheral Myelin Protein 22 (PMP22, Accession NM_000304). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMP22. Cyclin-dependent Kinase-like 2 (CDC2-related kinase) (CDKL2, Accession NM_003948) is another VGAM112 host target gene.

CDKL2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CDKL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKL2 BINDING SITE, designated SEQ ID:10070, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9418] Another function of VGAM112 is therefore inhibition of Cyclin-dependent Kinase-like 2 (CDC2-related kinase) (CDKL2, Accession NM_003948). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKL2. FLJ21290 (Accession NM_025034) is another VGAM112 host target gene. FLJ21290 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21290 BINDING SITE, designated SEQ ID:24633, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2823.

[9419] Another function of VGAM112 is therefore inhibition of FLJ21290 (Accession NM_025034). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21290. HSPC065 (Accession NM_014157) is another VGAM112 host target gene. HSPC065 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15453, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9420] Another function of VGAM112 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. KIAA1796 (Accession XM_166146) is another VGAM112 host target gene. KIAA1796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1796, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1796 BINDING SITE, designated SEQ ID:43963, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9421] Another function of VGAM112 is therefore inhibition of KIAA1796 (Accession XM_166146). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1796. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863) is another VGAM112 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11271, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9422] Another function of VGAM112 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2

(SPTLC2, Accession NM_004863). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. ZFD25 (Accession NM_016220) is another VGAM112 host target gene. ZFD25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFD25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFD25 BINDING SITE, designated SEQ ID:18320, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9423] Another function of VGAM112 is therefore inhibition of ZFD25 (Accession NM_016220). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFD25. LOC146435 (Accession XM_085465) is another VGAM112 host target gene. LOC146435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC146435 BINDING SITE, designated SEQ ID:38152, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9424] Another function of VGAM112 is therefore inhibition of LOC146435 (Accession XM_085465). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146435. LOC148709 (Accession XM_086281) is another VGAM112 host target gene. LOC148709 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148709 BINDING SITE, designated SEQ ID:38581, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9425] Another function of VGAM112 is therefore inhibition of LOC148709 (Accession XM_086281). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148709. LOC164955 (Accession XM_092265) is an-

other VGAM112 host target gene. LOC164955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164955 BINDING SITE, designated SEQ ID:40111, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9426] Another function of VGAM112 is therefore inhibition of LOC164955 (Accession XM_092265). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164955. LOC219627 (Accession XM_166402) is another VGAM112 host target gene. LOC219627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219627 BINDING SITE, designated SEQ ID:44273, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9427] Another function of VGAM112 is therefore inhibition of LOC219627 (Accession XM_166402). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219627. LOC220906 (Accession XM_166133) is another VGAM112 host target gene. LOC220906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220906 BINDING SITE, designated SEQ ID:43925, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9428] Another function of VGAM112 is therefore inhibition of LOC220906 (Accession XM_166133). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220906. LOC221312 (Accession XM_166314) is another VGAM112 host target gene. LOC221312 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221312, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221312 BINDING SITE, designated SEQ ID:44137, to the nucleotide sequence of VGAM112 RNA, herein designated VGAM RNA, also designated SEQ ID:2823.

[9429] Another function of VGAM112 is therefore inhibition of LOC221312 (Accession XM_166314). Accordingly, utilities of VGAM112 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221312. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 113 (VGAM113) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9430] VGAM113 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM113 was detected is described hereinabove with reference to Figs. 1–8.

[9431] VGAM113 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM113 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9432] VGAM113 gene encodes a VGAM113 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM113 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM113 precursor RNA is designated SEQ ID:99, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:99 is located at position 142719 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9433] VGAM113 precursor RNA folds onto itself, forming VGAM113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9434] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM113 folded precursor RNA into VGAM113 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM113 RNA is designated SEQ ID:2824, and is provided hereinbelow with reference to the sequence listing part.

[9435] VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM113 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9436] VGAM113 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM113 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM113 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9437] The complementary binding of VGAM113 RNA, herein designated VGAM RNA, to host target binding sites on VGAM113 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM113 host target RNA into VGAM113 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9438] It is appreciated that VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM113 host target genes. The mRNA of each one of this plurality of VGAM113 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM113 RNA, herein designated VGAM RNA, and which when bound by VGAM113 RNA causes inhibition of translation of respective one or more VGAM113 host target proteins.

[9439] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM113 gene, herein designated VGAM GENE, on one or more VGAM113 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9440] It is yet further appreciated that a function of VGAM113 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM113 correlate with, and may be deduced from, the identity of the host target genes which VGAM113 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9441] Nucleotide sequences of the VGAM113 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM113 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM113 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM113 are further

described hereinbelow with reference to Table 1.

[9442] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM113 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM113 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9443] As mentioned hereinabove with reference to Fig. 1, a function of VGAM113 gene, herein designated VGAM is inhibition of expression of VGAM113 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM113 correlate with, and may be deduced from, the identity of the target genes which VGAM113 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9444] Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 1; Cyclin D-related (CBFA2T1, Accession NM_004349) is a VGAM113 host target gene. CBFA2T1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of CBFA2T1 BINDING SITE, designated SEQ ID:10545, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9445] A function of VGAM113 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 1; Cyclin D-related (CBFA2T1, Accession NM_004349), a gene which produces a chimeric gene made up of the 5-prime region of the AML1 gene fused to the 3-prime region of the ETO gene through translocation. Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T1. The function of CBFA2T1 has been established by previous studies. Wolford and Prochazka (1998) reported that the MTG8 gene contains 13 exons spanning over 87 kb of DNA. They identified cDNAs representing alternatively spliced MTG8 transcripts in which a 155-bp exon (9a) is present. Inclusion of this exon changes the reading frame, resulting in the introduction of a premature stop codon. The encoded truncated proteins lack 177 C-terminal residues, which is the region containing 2 putative zinc finger motifs, the last P/

S/T-rich domain, and a putative alpha-helical coiled-coil structure. Northern blot analysis of human tissues detected an approximately 5.5-kb MTG8 transcript in heart, brain, placenta, lung, skeletal muscle, and pancreas but not in liver or kidney. RT-PCR analysis of a number of human tissues showed highest levels of MTG8 expression in fetal brain, followed by adult brain and heart. Relatively abundant mRNA levels were also found in lung, pituitary, and placenta. When first identified as a partner with AML1 in acute myeloid leukemia (Erickson et al., 1992; Miyoshi et al., 1993), the gene was referred to as MTG8 for 'myeloid translocation gene on 8q22.' Wolford et al. (1998) found that MTG8 mRNAs are expressed at relatively high levels in human adipose tissue. They therefore investigated MTG8 as a candidate gene in obesity, studying the relationship between a highly polymorphic marker in the 3-prime untranslated region of the MTG8 gene and obesity in Pima Indians of Arizona, a population with one of the highest reported rates of obesity. They detected a male-specific association with age-adjusted percentage body fat ($p = 0.0002$), body mass index ($p = 0.01$), waist circumference ($p = 0.008$), and thigh circumference ($p = 0.02$). Comparative analysis of all 13 MTG8 exons in 30

Pimas did not reveal any genetic variants that could explain the association with obesity in males.

[9446] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9447] Wolford, J. K.; Prochazka, M. : Structure and expression of the human MTG8/ETO gene. Gene 212: 103–109, 1998. ; and

[9448] Miyoshi, H.; Kozu, T.; Shimizu, K.; Enomoto, K.; Maseki, N.; Kaneko, Y.; Kamada, N.; Ohki, M. : The t(8;21) translocation in acute myeloid leukemia results in production of an AML1–MTG8.

[9449] Further studies establishing the function and utilities of CBFA2T1 are found in John Hopkins OMIM database record ID 133435, and in cited publications numbered 3447–3448, 3452–3453, 3449–345 and 3454–3459 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glycyl–tRNA Synthetase (GARS, Accession NM_002047) is another VGAM113 host target gene. GARS BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GARS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GARS BINDING SITE, designated SEQ ID:7798, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9450] Another function of VGAM113 is therefore inhibition of Glycyl-tRNA Synthetase (GARS, Accession NM_002047), a gene which functions in protein biosynthesis. Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GARS. The function of GARS has been established by previous studies. Aminoacyl-tRNA synthetases perform an essential function in protein synthesis by catalyzing the esterification of an amino acid to its cognate tRNA. These enzymes are necessarily present in each cell and must properly recognize the tRNA and the amino acid in order to maintain fidelity of translation. From the primary structures, 2 distinct classes of synthetases have been recognized, with similarity of certain structural features, amino acid attachment sites, and other properties between members of a class. Certain aminoacyl-tRNA synthetases are autoantigens in patients with the idiopathic inflammatory myopathies, polymyositis, and dermatomyositis. Au-

to antibodies reactive with synthetases are found almost exclusively in these conditions, with individuals usually having autoantibodies to only a single synthetase. Most commonly they are directed at histidyl-tRNA synthetase (OMIM Ref. No. 142810), labeled 'anti-Jo-1' autoantibodies. Ge et al. (1994) used a cDNA encoding the human form of glycyl-tRNA synthetase for isolation of corresponding cDNAs. Shiba et al. (1994) likewise cloned a class II human glycyl-tRNA synthetase and compared its structure with that of the bacterial counterpart from which it was found to diverge widely. Williams et al. (1995) also cloned the human GARS cDNA. The predicted 685-amino acid protein showed approximately 45% identity to the yeast protein. The recombinantly expressed protein was immunoprecipitated with human serum containing autoantibodies to glycyl-tRNA synthetase and was shown to catalyze the aminoacylation of tRNA.

[9451] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9452] Ge, Q.; Trieu, E. P.; Targoff, I. N. : Primary structure and functional expression of human glycyl-tRNA synthetase, an autoantigen in myositis. J. Biol. Chem. 269:

28790–28797, 1994. ; and

[9453] Nichols, R. C.; Pai, S. I.; Ge, Q.; Targoff, I. N.; Plotz, P. H.; Liu, P. : Localization of two human autoantigen genes by PCR screening and in situ hybridization--Glycyl-tRNA synthetase.

[9454] Further studies establishing the function and utilities of GARS are found in John Hopkins OMIM database record ID 600287, and in cited publications numbered 10119–10122 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Norrie Disease (pseudoglioma) (NDP, Accession NM_000266) is another VGAM113 host target gene. NDP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDP BINDING SITE, designated SEQ ID:5811, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9455] Another function of VGAM113 is therefore inhibition of Norrie Disease (pseudoglioma) (NDP, Accession NM_000266), a gene which may be involved in a pathway

that regulates neural cell differentiation and proliferation. Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDP. The function of NDP has been established by previous studies. Moreira-Filho and Neustein (1979) described 6 brothers with what they viewed as a variant of ND, because microcephaly was present in all. (In some ways the patients resembled those reported by Goldberg and McKusick as discussed in entry 309800.) The pedigree was informative for linkage with Xg; negative lod scores were obtained. Warburg et al. (1965) had demonstrated no linkage with the Xg blood groups. Johnston et al. (1982) described 2 families with 8 affected males--the first families reported from Ireland. Harendra de Silva and de Silva (1988) described an extensively affected family in Sri Lanka. Gal et al. (1985) found close linkage of Norrie disease to the L1.28/TaqI RFLP, DXS7 (maximum lod = 3.50 at theta = 0.00). Thus, ND may be in or slightly proximal to band Xp11.3 and near the retinitis pigmentosa locus (OMIM Ref. No. 312600), which is also linked to DXS7. Gal et al. (1985) found a peak lod score of 4.1 at theta 0.00 for linkage with DXS7; no recombination was found. DXS7 has been localized to

Xp11.3 (or Xp11.3–p11.2). See Bleeker–Wagemakers et al. (1985) for the full data. Gal et al. (1985, 1986) also described a 14-year-old boy with a complex syndrome dominated by Norrie disease who appeared to have a small deletion involving DXS7 as well; seemingly, the deletion had been transmitted through 3 generations. Other features of the complex were severe mental retardation, hypogonadism, growth disturbances, and increased susceptibility to infections. De la Chapelle et al. (1985) found a deletion defined by DXS7 in 4 affected members of a family. Using probe L1.28 in the study of a chorion villus sample, they could show that the male fetus of a carrier woman was unaffected. Kivlin et al. (1987) presented further linkage data. They stated that no recombination had been identified between ND and the DNA marker L1.28; with their data, the total lod score became 5.42. Ohba and Yamashita (1986) presented evidence suggesting that the Norrie disease locus may be on Xp at band Xp11. A female infant with typical clinical and histopathologic features of vitreoretinal dysplasia was found to have a reciprocal translocation at $t(X;10)(p11;p14)$. Her parents and sibs had normal karyotypes. Donnai et al. (1988) found that the DXS7 locus

was deleted in 2 affected brothers; DXS7 is located in Xp11.3. OTC (OMIM Ref. No. 311250), located at Xp21.1, and DXS84, also located at Xp21.1, were intact. Ngo et al. (1988) and Katayama et al. (1988) found the first recombinant between Norrie disease and the DXS7 locus. The addition of their family brought a total of published informative families to 7, with a maximum lod score of 7.58 at a recombination fraction of 0.038. They stated the assignment of the DXS7 locus (defined by probe L1.28) as Xp11.3-p11.2. Ngo et al. (1989) pointed out that a single recombination event had been reported twice (Ngo et al., 1988; Katayama et al., 1988); otherwise, a distorted impression of the distance between the marker and Norrie disease might be given. Gal et al. (1988) described prenatal exclusion with flanking DNA markers. In an addendum, they stated that 3 families with Norrie disease and DXS7 deletion had been reported, bringing the compiled lod score for NDP vs DXS7 linkage to 11.18 at $\theta = 0.00$. Using a RFLP detected by the ornithine amino transferase (OAT)-related DNA sequences that map to Xp (see OMIM Ref. No. 258870), Ngo et al. (1989) found a suggestion of linkage to the Norrie disease locus. In 3 generations of a family with 4 affected males in 3 sibships of 2 genera-

tions, Zhu et al. (1989) demonstrated deletion of 2 loci, DXS7 and DXS77. DNA studies of chorion villus biopsy material from the fetus of an obligatory carrier indicated that the fetus had inherited the normal allele from the carrier mother. This prediction was confirmed on eye examination at age 5 months. Deletions at the DXS7 locus have been detected in 3 other families (de la Chapelle et al., 1985; Gal et al., 1985; Donnai et al., 1988). Diergaarde et al. (1989) further refined the localization of the deletion in a Dutch case of ND. Sims et al. (1989) demonstrated that the Norrie disease gene is distinct from the monoamine oxidase genes, although some males with atypical Norrie disease who have a submicroscopic deletion in the region of the DXS7 locus have been shown to have disruption of the MAOA (OMIM Ref. No. 309850) and MAOB (OMIM Ref. No. 309860) genes. The authors studied genomic DNA from 19 males in 9 families affected with Norrie disease. No deletions or rearrangements in the region of DSX7 or MAOA were observed in the DNA of these patients. Linkage analysis between the NDP gene and the DSX7 or MAOA loci showed no recombination, with a lod score of 2.80 and 2.58 at a theta of 0.0 for MAOA and DSX7, respectively. MAO activities in fibroblasts and

platelets were normal. Although the MAO and NDP loci appear to be distinct, the high level of polymorphism at the MAO locus should prove useful in the molecular diagnosis of the disease. Collins et al. (1992) reported a male with Norrie disease and 2 obligate heterozygous females who were shown to have a submicroscopic deletion involving the Norrie disease locus and the loci for MAOA and MAOB. The propositus was a profoundly retarded, blind male; he also had neurologic abnormalities including myoclonus and stereotypy-habit disorder (persistent stereotypic and self-injurious behavior with a deleterious effect on the patient's adaptation to home and school environments). Both obligate carriers had a normal IQ. In the propositus, MAO activity was undetectable; in the female heterozygotes, the levels were reduced to the range observed in patients receiving MAO-inhibiting antidepressants. One of the carriers, the mother of the propositus, met diagnostic criteria for 'chronic hypomania and schizotypal features.' Lindsay et al. (1992) did linkage studies using a highly informative microsatellite marker, DXS426, which maps proximal to DXS7 in the interval Xp11.4-p11.23. A multiply informative crossover localized the NDP gene proximal to DXS7. In conjunction with infor-

mation from 2 NDP patients who had a deletion for DXS7 but not for DXS426, their data indicated that the NDP gene is between DXS7 and DXS426 on proximal Xp. Wolff et al. (1992) restudied the family with Episkopi blindness originally studied by Taylor et al. (1959). DNA studies revealed no deletion of any of the probes from proximal Xq. Linkage analysis yielded positive lod scores for all informative markers; e.g., with DXS255, maximum lod = 6.54 at $\theta = 0.0$. The findings confirmed that Episkopi blindness and Norrie disease are the same entity. Although Berger et al. (1992) and Chen et al. (1992) could identify no strong homologies with the candidate gene they identified, by studying the number and spacing of cysteine residues, Meindl et al. (1992) later detected homologies between the Norrie disease gene product and a C-terminal domain that is common to a group of proteins including mucins. Furthermore, they characterized 3 missense mutations, replacing evolutionarily conserved cysteines or creating new cysteine codons, emphasizing the functional importance of these sites. These findings and the clinical features of Norrie disease suggested a possible role for the NDP gene in a neuroectodermal cell-cell interaction. Only exons 2 and 3 of the NDP gene are

translated. Exon 2 contains the first 58 codons of the open reading frame. The intron that follows it is roughly 14.5 kb. Exon 3 is the largest exon and contains residues 59–133 of the open reading frame and a 917-bp untranslated 3-prime-region. Chen et al. (1993) isolated genomic DNA clones encompassing the NDP gene which they found spans 28 kb and consists of 3 exons, the first of which is entirely contained within the 5-prime untranslated region. By PCR analysis, they found that expression of the NDP gene is not confined to the eye or to the brain. They found homology with cysteine-rich protein-binding domains of intermediate-early genes implicated in the regulation of cell proliferation. This led them to propose that the NDP molecule likewise may be involved in the pathway that regulates neural cell differentiation and proliferation. Meitinger et al. (1993) reported that sequence pattern searches and 3-dimensional modeling suggested that the Norrie disease protein (NDP) has a tertiary structure similar to that of a transforming growth factor beta (e.g., 190180). The model identified NDP as a member of an emerging family of growth factors containing a cystine knot motif, with direct implications for the physiologic role of NDP.

- [9456] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9457] de la Chapelle, A.; Sankila, E.-M.; Lindlof, M.; Aula, P.; Norio, R. : Norrie disease caused by a gene deletion allowing carrier detection and prenatal diagnosis. Clin. Genet. 28: 317-320, 1985. ; and
- [9458] Meitinger, T.; Meindl, A.; Bork, P.; Rost, B.; Sander, C.; Haasemann, M.; Murken, J. : Molecular modeling of the Norrie disease protein predicts a cystine knot growth factor tertiary st.
- [9459] Further studies establishing the function and utilities of NDP are found in John Hopkins OMIM database record ID 310600, and in cited publications numbered 8614-8617, 2931, 8800, 10615-2936, 1867, 2937, 2945, 9179-2940, 10616-2944, 2946-2949, 10697, 8125, 8127-8145, 1469, 8146-8151, 9180-8155, 8363, 8372-837 and 8807-8381 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ11101 (Accession NM_018322) is another VGAM113 host target gene. FLJ11101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11101, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11101 BINDING SITE, designated SEQ ID:20315, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9460] Another function of VGAM113 is therefore inhibition of FLJ11101 (Accession NM_018322). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11101. FLJ13072 (Accession XM_117117) is another VGAM113 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43236, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9461] Another function of VGAM113 is therefore inhibition of FLJ13072 (Accession XM_117117). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ13072. FLJ20729 (Accession NM_017953) is another VGAM113 host target gene. FLJ20729 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20729, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20729 BINDING SITE, designated SEQ ID:19658, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9462] Another function of VGAM113 is therefore inhibition of FLJ20729 (Accession NM_017953). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20729. FLJ20802 (Accession NM_017959) is another VGAM113 host target gene. FLJ20802 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20802, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20802 BINDING SITE, designated SEQ ID:19674, to the nucleotide sequence of

VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9463] Another function of VGAM113 is therefore inhibition of FLJ20802 (Accession NM_017959). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20802. FLJ22169 (Accession NM_024085) is another VGAM113 host target gene. FLJ22169 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22169 BINDING SITE, designated SEQ ID:23523, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9464] Another function of VGAM113 is therefore inhibition of FLJ22169 (Accession NM_024085). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22169. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM113 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7863, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9465] Another function of VGAM113 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. KIAA0014 (Accession NM_014665) is another VGAM113 host target gene. KIAA0014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0014 BINDING SITE, designated SEQ ID:16118, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9466] Another function of VGAM113 is therefore inhibition of KIAA0014 (Accession NM_014665). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0014. KIAA0494 (Accession NM_014774) is another VGAM113 host target gene. KIAA0494 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0494, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0494 BINDING SITE, designated SEQ ID:16593, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9467] Another function of VGAM113 is therefore inhibition of KIAA0494 (Accession NM_014774). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0494. MAP (Accession NM_022818) is another VGAM113 host target gene. MAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP BINDING SITE, designated SEQ ID:23096, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9468] Another function of VGAM113 is therefore inhibition of MAP (Accession NM_022818). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP. NIR3 (Accession XM_038799) is another VGAM113 host target gene. NIR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NIR3 BINDING SITE, designated SEQ ID:32927, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9469] Another function of VGAM113 is therefore inhibition of NIR3 (Accession XM_038799). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIR3. LOC160156 (Accession XM_090047) is another VGAM113

host target gene. LOC160156 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160156 BINDING SITE, designated SEQ ID:39992, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9470] Another function of VGAM113 is therefore inhibition of LOC160156 (Accession XM_090047). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160156. LOC220477 (Accession XM_071675) is another VGAM113 host target gene. LOC220477 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220477 BINDING SITE, designated SEQ ID:37408, to the nucleotide sequence of VGAM113 RNA, herein designated VGAM RNA, also designated SEQ ID:2824.

[9471] Another function of VGAM113 is therefore inhibition of LOC220477 (Accession XM_071675). Accordingly, utilities of VGAM113 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220477. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 114 (VGAM114) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9472] VGAM114 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM114 was detected is described hereinabove with reference to Figs. 1–8.

[9473] VGAM114 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9474] VGAM114 gene encodes a VGAM114 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM114

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM114 precursor RNA is designated SEQ ID:100, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:100 is located at position 41311 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9475] VGAM114 precursor RNA folds onto itself, forming VGAM114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9476] An enzyme complex designated DICER COMPLEX, `dices` the VGAM114 folded precursor RNA into VGAM114 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM114 RNA is designated SEQ ID:2825, and is provided hereinbelow with reference to the sequence listing part.

[9477] VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM114 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9478] VGAM114 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM114 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM114 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[9479] The complementary binding of VGAM114 RNA, herein designated VGAM RNA, to host target binding sites on VGAM114 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM114 host target RNA into VGAM114 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9480] It is appreciated that VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM114 host target genes. The mRNA of

each one of this plurality of VGAM114 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM114 RNA, herein designated VGAM RNA, and which when bound by VGAM114 RNA causes inhibition of translation of respective one or more VGAM114 host target proteins.

[9481] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM114 gene, herein designated VGAM GENE, on one or more VGAM114 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[9482] It is yet further appreciated that a function of VGAM114 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM114 correlate with, and may be deduced from, the identity of the host target genes which VGAM114 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9483] Nucleotide sequences of the VGAM114 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM114 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM114 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM114 are further described hereinbelow with reference to Table 1.

[9484] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM114 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM114 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9485] As mentioned hereinabove with reference to Fig. 1, a function of VGAM114 gene, herein designated VGAM is inhibition of expression of VGAM114 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM114 correlate with, and may be deduced from, the identity of the target genes which VGAM114 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9486] Adenylate Cyclase 7 (ADCY7, Accession NM_001114) is a VGAM114 host target gene. ADCY7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ADCY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY7 BINDING SITE, designated SEQ ID:6783, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9487] A function of VGAM114 is therefore inhibition of Adenylate Cyclase 7 (ADCY7, Accession NM_001114), a gene

which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY7. The function of ADCY7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM108. Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM_000723) is another VGAM114 host target gene. CACNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNB1 BINDING SITE, designated SEQ ID:6385, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9488] Another function of VGAM114 is therefore inhibition of Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM_000723), a gene which may not only play an important role in the transport/insertion of the alpha-1S subunit into the membrane. Accordingly,

utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNB1. The function of CACNB1 has been established by previous studies. Pragnell et al. (1991) isolated a cDNA clone encoding a protein with high homology to the beta subunit of the rabbit skeletal muscle dihydropyridine-sensitive calcium channel from a rat brain cDNA library. This rat brain beta-subunit cDNA hybridized to a 3.4-kb message that was expressed in high levels in the cerebral hemispheres and hippocampus and much lower levels in cerebellum. The open reading frame encodes 597 amino acids with a predicted mass of 65,679 Da which is 82% homologous with the skeletal muscle beta subunit. The corresponding human beta-subunit gene was localized to chromosome 17 by analysis of somatic cell hybrids. Pragnell et al. (1991) suggested that the encoded brain beta subunit, which has a primary structure highly similar to its isoform in skeletal muscle, may have a comparable role as an integral regulatory component of a neuronal calcium channel. To determine the role of the beta-1 subunit in channel activity and excitation-contraction coupling, Gregg et al. (1996) used gene targeting to inactivate the beta-1 subunit in mice. Homozygous

mutant fetuses had a phenotype very similar to that seen in mice with mutations in either the alpha-1S subunit ('muscular dysgenic') or in the ryanodine receptor-1 (OMIM Ref. No. 180901), 'skrr.' All 3 mutants lacked excitation-contraction coupling. Beta-1-null mice died at birth from asphyxia. Electrical stimulation of beta-1-muscle failed to induce twitches; however, contractures were induced by caffeine. In isolated beta-1-null myotubes, action potentials were normal but failed to elicit calcium ion transient. Immunohistochemistry of cultured myotubes showed that not only was the beta-1 subunit absent, but the amount of alpha-1S in the membrane was also undetectable. In contrast, the beta-1 subunit was appropriately localized in alpha-1S-null cells. Therefore, Gregg et al. (1996) concluded that the beta-1 subunit may not only play an important role in the transport/insertion of the alpha-1S subunit into the membrane, but may also be vital for the targeting of the muscle dihydropyridine receptor complex to the transverse tubule/sarcoplasmic reticulum junction.

[9489] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [9490] Pragnell, M.; Sakamoto, J.; Jay, S. D.; Campbell, K. P. : Cloning and tissue-specific expression of the brain calcium channel beta-subunit. FEBS Lett. 291: 253-258, 1991. ; and
- [9491] Gregg, R. G.; Messing, A.; Strube, C.; Beurg, M.; Moss, R.; Behan, M.; Sukhareva, M.; Haynes, S.; Powell, J. A.; Coronado, R.; Powers, P. A. : Absence of the beta subunit (cchb1) of the.
- [9492] Further studies establishing the function and utilities of CACNB1 are found in John Hopkins OMIM database record ID 114207, and in cited publications numbered 4852-4853, 485 and 4854 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DEC1 (Accession NM_017418) is another VGAM114 host target gene. DEC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DEC1 BINDING SITE, designated SEQ ID:18875, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9493] Another function of VGAM114 is therefore inhibition of DEC1 (Accession NM_017418), a gene which acts as a tumor suppressor associated with esophageal cancer. Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DEC1. The function of DEC1 has been established by previous studies. Loss of heterozygosity (LOH) is often shown at 9q31 in esophageal squamous cell carcinomas (OMIM Ref. No. 133239) as well as in squamous cell carcinomas of developmentally related tissues such as bladder (OMIM Ref. No. 109800), lung (OMIM Ref. No. 211980), and head and neck. Miura et al. (1996) delineated a region commonly deleted in esophageal squamous cell carcinomas to a 200-kb segment at 9q32. Nishiwaki et al. (2000) sequenced overlapping clones in this commonly deleted region and identified a possible candidate gene, which they named 'deleted in esophageal cancer-1' (DEC1). The DEC1 gene encodes a deduced 70-amino acid protein. Northern blot analysis detected a 1.4-kb DEC1 transcript in all tissues tested, with highest expression in prostate and testis. DEC1 expression was lower than normal and often absent in more than half of the esophageal carcinomas examined. Furthermore, DEC1

cDNA was able to exert growth suppressive activity in vitro. Although expression was reduced, no genetic alteration was detected in the DEC1 gene in any of the cancers examined.

[9494] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9495] Miura, K.; Suzuki, K.; Tokino, T.; Isomura, M.; Inazawa, J.; Matsuno, S.; Nakamura, Y. : Detailed deletion mapping in squamous cell carcinomas of the esophagus narrows a region containing a putative tumor suppressor gene to about 200 kilobases on distal chromosome 9q. *Cancer Res.* 56: 1629–1634, 1996. ; and

[9496] Nishiwaki, T.; Daigo, Y.; Kawasoe, T.; Nakamura, Y. : Isolation and mutational analysis of a novel human cDNA, DEC1 (deleted in esophageal cancer 1), derived from the tumor suppressor l.

[9497] Further studies establishing the function and utilities of DEC1 are found in John Hopkins OMIM database record ID 604767, and in cited publications numbered 7291–7292 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hippocalcin (HPCA, Accession NM_002143) is another VGAM114 host target

gene. HPCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCA BINDING SITE, designated SEQ ID:7919, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9498] Another function of VGAM114 is therefore inhibition of Hippocalcin (HPCA, Accession NM_002143), a gene which may be an hippocampal calcium-binding protein. Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCA. The function of HPCA has been established by previous studies. Hippocalcin is a member of a family of neuron-specific $\text{Ca}(2+)$ -binding proteins found in the retina and brain. Hippocalcin is a 23-kD $\text{Ca}(2+)$ -binding protein first identified in the rat hippocampus (Kobayashi et al., 1992). The primary structure of rat hippocalcin comprises 193 amino acid residues and shows striking sequence similarities to proteins located in the photoreceptor cells that regulate photosignal transduction in a $\text{Ca}(2+)$ -sensitive manner. Hippocalcin is as-

sociated with the plasma membrane. Takamatsu et al. (1994) isolated a cDNA clone encoding human hippocalcin from a human hippocampus cDNA library. The human sequence showed 100% amino acid identity with the rat sequence and 92% nucleotide identity. Northern blot analysis detected a single 2.0-kb HPCA transcript only in brain.

[9499] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9500] Kobayashi, M.; Takamatsu, K.; Saitoh, S.; Miura, M.; Noguchi, T. : Molecular cloning of hippocalcin, a novel calcium-binding protein of the recoverin family exclusively expressed in hippocampus. *Biochem. Biophys. Res. Commun.* 189: 511-517, 1992. ; and

[9501] Takamatsu, K.; Kobayashi, M.; Saitoh, S.; Fujishiro, M.; Noguchi, T. : Molecular cloning of human hippocalcin cDNA and chromosomal mapping of its gene. *Biochem. Biophys. Res. Commun.* 20.

[9502] Further studies establishing the function and utilities of HPCA are found in John Hopkins OMIM database record ID 142622, and in cited publications numbered 3893-3894 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kell Blood Group

Precursor (McLeod phenotype) (XK, Accession NM_021083) is another VGAM114 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22057, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9503] Another function of VGAM114 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. DKFZp547I224 (Accession NM_020221) is another VGAM114 host target gene. DKFZp547I224 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547I224, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I224 BINDING SITE, designated SEQ ID:21480, to the nucleotide se-

quence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9504] Another function of VGAM114 is therefore inhibition of DKFZp547I224 (Accession NM_020221). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I224. DKFZP564D0478 (Accession NM_032125) is another VGAM114 host target gene. DKFZP564D0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D0478 BINDING SITE, designated SEQ ID:25810, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9505] Another function of VGAM114 is therefore inhibition of DKFZP564D0478 (Accession NM_032125). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D0478. FLJ12572 (Accession NM_022905) is another VGAM114 host target gene. FLJ12572 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12572, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12572 BINDING SITE, designated SEQ ID:23201, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9506] Another function of VGAM114 is therefore inhibition of FLJ12572 (Accession NM_022905). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12572. Hypermethylated In Cancer 2 (HIC2, Accession XM_036937) is another VGAM114 host target gene. HIC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIC2 BINDING SITE, designated SEQ ID:32525, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9507] Another function of VGAM114 is therefore inhibition of

Hypermethylated In Cancer 2 (HIC2, Accession XM_036937). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIC2. HSA243666 (Accession NM_017582) is another VGAM114 host target gene. HSA243666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA243666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA243666 BINDING SITE, designated SEQ ID:19022, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9508] Another function of VGAM114 is therefore inhibition of HSA243666 (Accession NM_017582). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA243666. KIAA0296 (Accession NM_014699) is another VGAM114 host target gene. KIAA0296 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0296, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0296 BINDING SITE, designated SEQ ID:16218, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9509] Another function of VGAM114 is therefore inhibition of KIAA0296 (Accession NM_014699). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0296. LEAP-2 (Accession NM_052971) is another VGAM114 host target gene. LEAP-2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LEAP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEAP-2 BINDING SITE, designated SEQ ID:27545, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9510] Another function of VGAM114 is therefore inhibition of LEAP-2 (Accession NM_052971). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEAP-2.

MGC10715 (Accession NM_024325) is another VGAM114 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23613, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9511] Another function of VGAM114 is therefore inhibition of MGC10715 (Accession NM_024325). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. SARM (Accession NM_015077) is another VGAM114 host target gene. SARM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SARM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SARM BINDING SITE, designated SEQ ID:17455, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2825.

[9512] Another function of VGAM114 is therefore inhibition of SARM (Accession NM_015077). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SARM. LOC143287 (Accession XM_096410) is another VGAM114 host target gene. LOC143287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143287 BINDING SITE, designated SEQ ID:40344, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9513] Another function of VGAM114 is therefore inhibition of LOC143287 (Accession XM_096410). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143287. LOC150967 (Accession XM_087060) is another VGAM114 host target gene. LOC150967 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150967, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150967 BINDING SITE, designated SEQ ID:39036, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9514] Another function of VGAM114 is therefore inhibition of LOC150967 (Accession XM_087060). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150967. LOC154877 (Accession XM_098626) is another VGAM114 host target gene. LOC154877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154877 BINDING SITE, designated SEQ ID:41745, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9515] Another function of VGAM114 is therefore inhibition of LOC154877 (Accession XM_098626). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC154877. LOC165904 (Accession XM_093522) is another VGAM114 host target gene. LOC165904 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC165904, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165904 BINDING SITE, designated SEQ ID:40193, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9516] Another function of VGAM114 is therefore inhibition of LOC165904 (Accession XM_093522). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165904. LOC200325 (Accession XM_117223) is another VGAM114 host target gene. LOC200325 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200325, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200325 BINDING SITE, designated SEQ ID:43288, to

the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9517] Another function of VGAM114 is therefore inhibition of LOC200325 (Accession XM_117223). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200325. LOC206463 (Accession XM_116523) is another VGAM114 host target gene. LOC206463 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC206463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206463 BINDING SITE, designated SEQ ID:43122, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9518] Another function of VGAM114 is therefore inhibition of LOC206463 (Accession XM_116523). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206463. LOC220469 (Accession XM_084334) is another VGAM114 host target gene. LOC220469 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220469 BINDING SITE, designated SEQ ID:37555, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9519] Another function of VGAM114 is therefore inhibition of LOC220469 (Accession XM_084334). Accordingly, utilities of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220469. LOC245806 (Accession XM_166309) is another VGAM114 host target gene. LOC245806 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC245806, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245806 BINDING SITE, designated SEQ ID:44130, to the nucleotide sequence of VGAM114 RNA, herein designated VGAM RNA, also designated SEQ ID:2825.

[9520] Another function of VGAM114 is therefore inhibition of LOC245806 (Accession XM_166309). Accordingly, utilities

of VGAM114 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245806. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 115 (VGAM115) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9521] VGAM115 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM115 was detected is described hereinabove with reference to Figs. 1–8.

[9522] VGAM115 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9523] VGAM115 gene encodes a VGAM115 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM115 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM115 precursor RNA is designated SEQ ID:101, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:101 is located at position 125173 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9524] VGAM115 precursor RNA folds onto itself, forming VGAM115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9525] An enzyme complex designated DICER COMPLEX, `dices` the VGAM115 folded precursor RNA into VGAM115 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 82%) nucleotide se-

quence of VGAM115 RNA is designated SEQ ID:2826, and is provided hereinbelow with reference to the sequence listing part.

[9526] VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM115 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[9527] VGAM115 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM115 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM115 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[9528] The complementary binding of VGAM115 RNA, herein designated VGAM RNA, to host target binding sites on VGAM115 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM115 host target RNA into VGAM115 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9529] It is appreciated that VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM115 host target genes. The mRNA of each one of this plurality of VGAM115 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM115 RNA, herein designated VGAM RNA, and which when bound by VGAM115 RNA causes inhibition of translation of respective one or more VGAM115 host target proteins.

[9530] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM115 gene, herein designated VGAM GENE, on one or more VGAM115 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9531] It is yet further appreciated that a function of VGAM115 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM115 correlate with, and may be deduced from, the identity of the host target genes which VGAM115 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9532] Nucleotide sequences of the VGAM115 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM115 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM115 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM115 are further described hereinbelow with reference to Table 1.

[9533] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM115 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM115 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[9534] As mentioned hereinabove with reference to Fig. 1, a function of VGAM115 gene, herein designated VGAM is inhibition of expression of VGAM115 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM115 correlate with, and may be deduced from, the identity of the target genes which VGAM115 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9535] General Transcription Factor II, I (GTF2I, Accession NM_032999) is a VGAM115 host target gene. GTF2I BINDING SITE1 and GTF2I BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GTF2I, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF2I BINDING SITE1 and GTF2I BINDING SITE2, designated SEQ ID:26883 and SEQ ID:26887 respectively, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9536] A function of VGAM115 is therefore inhibition of General Transcription Factor II, I (GTF2I, Accession NM_032999), a

gene which interacts with the basal transcription machinery by coordinating the formation of a multiprotein complex at the c-fos promoter, and linking specific signal responsive activator complexes. Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF2I. The function of GTF2I has been established by previous studies. Through transfection experiments, Roy et al. (1997) found that GTF2I is capable of binding to both a pyrimidine-rich initiator (Inr) and an E-box for upstream stimulatory factor-1 (USF1; 191523). GTF2I and USF1 can also act synergistically to activate transcription through both Inr and the E-box elements of the adenovirus major late promoter. By in vitro cotranslation followed by coimmunoprecipitation studies, Roy et al. (1997) confirmed direct protein interaction between GTF2I and USF1.

Williams-Beuren syndrome (WBS; 194050) is a neurodevelopmental disorder with multisystemic manifestations caused by heterozygosity for a partial deletion of 7q11.23. The breakpoints cluster within regions located approximately 1 cM at either side of the elastin locus (ELN; 130160). Perez Jurado et al. (1998) characterized a duplicated region near the common deletion breakpoints,

which includes a transcribed gene. The centromeric (C) and telomeric (T) copies are almost identical in the duplicated 3-prime portions but diverge at the 5-prime ends. C-specific 4.3-kb mRNA and T-specific 5.4-kb mRNA are widely expressed in embryonic and adult tissues. The telomeric gene gives rise to several tandemly spliced forms and is deleted in all WBS individuals who have documented ELN deletions. Database searches showed that this gene encodes BAP135, a protein phosphorylated by BTK in B cells, as well as the multifunctional transcription factor TFII-I; hence, the gene name GTF2I. The centromeric gene is not deleted in WBS and appears to be a partially truncated expressed pseudogene (GTF2IP1) with no protein product. Both loci map to different genomic clone contigs that also contain other deleted and non-deleted loci. The duplicated region containing GTF2I and GTF2IP1, respectively, is located close to the deletion breakpoints and may predispose to unequal meiotic recombination between chromosome 7 homologs and/or to intrachromosomal rearrangements. Hemizyosity for GTF2I may also contribute to the WBS phenotype.

[9537] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [9538] Perez Jurado, L. A.; Wang, Y.-K.; Peoples, R.; Coloma, A.; Cruces, J.; Francke, U. : A duplicated gene in the break-point regions of the 7q11.23 Williams-Beuren syndrome deletion encodes the initiator binding protein TFII-I and BAP-135, a phosphorylation target of BTK. Hum. Molec. Genet. 7: 325-334, 1998. ; and
- [9539] Roy, A. L.; Du, H.; Gregor, P. D.; Novina, C. D.; Martinez, E.; Roeder, R. G. : Cloning of an Inr- and E-box binding protein, TFII-I, that interacts physically and functionally with USF1.
- [9540] Further studies establishing the function and utilities of GTF2I are found in John Hopkins OMIM database record ID 601679, and in cited publications numbered 619 and 12616 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM_003053) is another VGAM115 host target gene. SLC18A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC18A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SLC18A1 BINDING SITE, designated SEQ ID:9017, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9541] Another function of VGAM115 is therefore inhibition of Solute Carrier Family 18 (vesicular monoamine), Member 1 (SLC18A1, Accession NM_003053), a gene which is involved in the vesicular transport of biogenic amines. Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC18A1. The function of SLC18A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18.FLJ23563 (Accession XM_041701) is another VGAM115 host target gene. FLJ23563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23563 BINDING SITE, designated SEQ ID:33560, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ

ID:2826.

[9542] Another function of VGAM115 is therefore inhibition of FLJ23563 (Accession XM_041701). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23563. KIAA0408 (Accession NM_014702) is another VGAM115 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16232, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9543] Another function of VGAM115 is therefore inhibition of KIAA0408 (Accession NM_014702). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. KIAA0527 (Accession XM_171054) is another VGAM115 host target gene. KIAA0527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0527, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0527 BINDING SITE, designated SEQ ID:45844, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9544] Another function of VGAM115 is therefore inhibition of KIAA0527 (Accession XM_171054). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0527. KIAA1535 (Accession XM_086565) is another VGAM115 host target gene. KIAA1535 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1535 BINDING SITE, designated SEQ ID:38765, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9545] Another function of VGAM115 is therefore inhibition of KIAA1535 (Accession XM_086565). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1535. MGC13007 (Accession NM_032320) is another VGAM115 host target gene. MGC13007 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC13007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13007 BINDING SITE, designated SEQ ID:26120, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9546] Another function of VGAM115 is therefore inhibition of MGC13007 (Accession NM_032320). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13007. RNA Binding Motif Protein 14 (RBM14, Accession NM_006328) is another VGAM115 host target gene. RBM14 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RBM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RBM14 BINDING SITE, designated SEQ

ID:13020, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9547] Another function of VGAM115 is therefore inhibition of RNA Binding Motif Protein 14 (RBM14, Accession NM_006328). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RBM14. LOC147343 (Accession XM_097225) is another VGAM115 host target gene. LOC147343 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147343, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147343 BINDING SITE, designated SEQ ID:40831, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9548] Another function of VGAM115 is therefore inhibition of LOC147343 (Accession XM_097225). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147343. LOC149301 (Accession XM_086480) is an-

other VGAM115 host target gene. LOC149301 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149301 BINDING SITE, designated SEQ ID:38690, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9549] Another function of VGAM115 is therefore inhibition of LOC149301 (Accession XM_086480). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149301. LOC257319 (Accession XM_171049) is another VGAM115 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45831, to the nucleotide sequence of VGAM115 RNA, herein designated VGAM RNA, also designated SEQ ID:2826.

[9550] Another function of VGAM115 is therefore inhibition of LOC257319 (Accession XM_171049). Accordingly, utilities of VGAM115 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 116 (VGAM116) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9551] VGAM116 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM116 was detected is described hereinabove with reference to Figs. 1–8.

[9552] VGAM116 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9553] VGAM116 gene encodes a VGAM116 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM116

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM116 precursor RNA is designated SEQ ID:102, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:102 is located at position 284651 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9554] VGAM116 precursor RNA folds onto itself, forming VGAM116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9555] An enzyme complex designated DICER COMPLEX, `dices` the VGAM116 folded precursor RNA into VGAM116 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM116 RNA is designated SEQ ID:2827, and is provided hereinbelow with reference to the sequence listing part.

[9556] VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM116 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[9557] VGAM116 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM116 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM116 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[9558] The complementary binding of VGAM116 RNA, herein designated VGAM RNA, to host target binding sites on VGAM116 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM116 host target RNA into VGAM116 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9559] It is appreciated that VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM116 host target genes. The mRNA of

each one of this plurality of VGAM116 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM116 RNA, herein designated VGAM RNA, and which when bound by VGAM116 RNA causes inhibition of translation of respective one or more VGAM116 host target proteins.

[9560] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM116 gene, herein designated VGAM GENE, on one or more VGAM116 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[9561] It is yet further appreciated that a function of VGAM116 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM116 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM116 correlate with, and may be deduced from, the identity of the host target genes which VGAM116 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9562] Nucleotide sequences of the VGAM116 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM116 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM116 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM116 are further described hereinbelow with reference to Table 1.

[9563] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM116 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM116 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9564] As mentioned hereinabove with reference to Fig. 1, a function of VGAM116 gene, herein designated VGAM is inhibition of expression of VGAM116 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM116 correlate with, and may be deduced from, the identity of the target genes which VGAM116 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9565] Calnexin (CANX, Accession XM_113469) is a VGAM116 host target gene. CANX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CANX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CANX BINDING SITE, designated SEQ ID:42278, to the nucleotide sequence of VGAM116 RNA, herein designated VGAM RNA, also designated SEQ ID:2827.

[9566] A function of VGAM116 is therefore inhibition of Calnexin (CANX, Accession XM_113469), a gene which may func-

tion as a chaperone in the endoplasmic reticulum, involved in the secretion of proteins from the ER to the outer cellular membrane. Accordingly, utilities of VGAM116 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CANX. The function of CANX has been established by previous studies. Calnexin is a 90-kilodalton integral membrane protein of the endoplasmic reticulum (ER). It exhibits high affinity for the binding of calcium ions, which was the means by which it was first identified. Calcium ions are known to play a central role in the regulation of cellular metabolism, including signal transduction events and the transport of proteins through the ER. Calnexin has been shown to be associated with several cell surface proteins during translocation through the ER and has been isolated as a complex with other ER proteins involved in calcium ion-dependent retention of proteins. It may function as a chaperone to regulate the transit of proteins through the ER. Tjoelker et al. (1994) isolated cDNA clones of the human, mouse, and rat calnexins. Comparisons of the sequences demonstrated a high level of conservation of sequence identity, suggesting that calnexin performs important cellular functions. Schwann cell-derived peripheral

myelin protein-22 (PMP22; 601097), when mutated or overexpressed, causes heritable neuropathies with a 'gain-of-function' endoplasmic reticulum (ER) phenotype.

PMP22 associates in a specific and transient manner with CANX in wildtype sciatic nerves. In the sciatic nerves of the Trembler (TrJ) mouse carrying the same mutation in the PMP22 gene that causes Charcot-Marie-Tooth disease (CMT) in the human, Dickson et al. (2002) found prolonged association of mutant PMP22 with CANX. In cultured cells expressing the TrJ mutant PMP22, CANX and PMP22 colocalized in large intracellular structures identified at the electron microscopy level as myelin-like figures, with CANX localization in the structures dependent on PMP22 glucosylation. Similar intracellular myelin-like figures were also present in Schwann cells of sciatic nerves from homozygous TrJ mice. Sequestration of CANX in intracellular myelin-like figures may be relevant to the pathogenesis of autosomal dominant CMT-related neuropathies.

[9567] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9568] Tjoelker, L. W.; Seyfried, C. E.; Eddy, R. L., Jr.; Byers, M. G.;

Shows, T. B.; Calderon, J.; Schreiber, R. B.; Gray, P. W. :
Human, mouse, and rat calnexin cDNA cloning: identification of potential calcium binding motifs and gene localization to human chromosome 5. *Biochemistry* 33: 3229–3236, 1994. ; and

[9569] Dickson, K. M.; Bergeron, J. J. M.; Shames, I.; Colby, J.;
Nguyen, D. T.; Chevet, E.; Thomas, D. Y.; Snipes, G. J. :
Association of calnexin with mutant peripheral myelin
protein–22 ex v.

[9570] Further studies establishing the function and utilities of
CANX are found in John Hopkins OMIM database record ID
114217, and in cited publications numbered 4032–4035
listed in the bibliography section hereinbelow, which are
also hereby incorporated by reference. DKFZP564C196
(Accession XM_046405) is another VGAM116 host target
gene. DKFZP564C196 BINDING SITE is HOST TARGET
binding site found in the 3` untranslated region of mRNA
encoded by DKFZP564C196, corresponding to a HOST
TARGET binding site such as BINDING SITE I, BINDING SITE
II or BINDING SITE III. Table 2 illustrates the complemen-
tarity of the nucleotide sequences of DKFZP564C196
BINDING SITE, designated SEQ ID:34714, to the nucleotide
sequence of VGAM116 RNA, herein designated VGAM

RNA, also designated SEQ ID:2827.

- [9571] Another function of VGAM116 is therefore inhibition of DKFZP564C196 (Accession XM_046405). Accordingly, utilities of VGAM116 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564C196. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 117 (VGAM117) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [9572] VGAM117 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM117 was detected is described hereinabove with reference to Figs. 1–8.
- [9573] VGAM117 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [9574] VGAM117 gene encodes a VGAM117 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM117 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM117 precursor RNA is designated SEQ ID:103, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:103 is located at position 80462 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9575] VGAM117 precursor RNA folds onto itself, forming VGAM117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9576] An enzyme complex designated DICER COMPLEX, `dices` the VGAM117 folded precursor RNA into VGAM117 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM117 RNA is designated SEQ ID:2828, and is provided hereinbelow with reference to the sequence listing part.

[9577] VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM117 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[9578] VGAM117 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM117 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM117 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9579] The complementary binding of VGAM117 RNA, herein designated VGAM RNA, to host target binding sites on VGAM117 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM117 host target RNA into VGAM117 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9580] It is appreciated that VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM117 host target genes. The mRNA of each one of this plurality of VGAM117 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM117 RNA, herein designated VGAM RNA, and which when bound by VGAM117 RNA causes inhibition of translation of respective one or more VGAM117 host target proteins.

[9581] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM117 gene, herein designated VGAM GENE, on one or more VGAM117 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[9582] It is yet further appreciated that a function of VGAM117 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM117 correlate with, and may be deduced from, the identity of the host target genes which VGAM117 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9583] Nucleotide sequences of the VGAM117 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM117 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM117 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM117 are further described hereinbelow with reference to Table 1.

[9584] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM117 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM117 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9585] As mentioned hereinabove with reference to Fig. 1, a function of VGAM117 gene, herein designated VGAM is inhibition of expression of VGAM117 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM117 correlate with, and may be deduced from, the identity of the target genes which VGAM117 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9586] Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is a VGAM117 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12879, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, also designated SEQ ID:2828.

[9587] A function of VGAM117 is therefore inhibition of Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA has been established by previous studies. Considerable insight into the role of the sonic hedgehog (OMIM Ref. No. 600725) pathway in vertebrate development and human cancers came from the discovery that mutations in `patched` (PTCH; 601309) are associated with basal cell nevus syndrome (BCNS; 109400), an autosomal dominant disorder combining developmental anomalies and tumors, particularly basal cell carcinomas (BCCs). Sporadic BCCs, the most common human cancer, consistently have abnormalities in the hedgehog pathway, and often mutations in PTCH. In addition, somatic mutations in `smoothened` (SMOH; 601500), another protein in the hedgehog pathway, occur in sporadic BCCs. The downstream molecule GLI1 (OMIM Ref. No. 165220) is known to mediate the biologic effect of the hedgehog pathway and is itself upregulated in all BCCs. Gli1 can

drive the production of BCCs in the mouse when overexpressed in the epidermis. Xie et al. (2001) showed that GLI1 can activate PDGFR-alpha and that functional upregulation of PDGFR-alpha by GLI1 is accompanied by activation of the Ras-ERK pathway, which is associated with cell proliferation. The relevance of this mechanism in vivo is supported by a high level of expression of PDGFR-alpha in BCCs in mice and humans. From these and other observations, Xie et al. (2001) concluded that increased expression of the PDGFR-alpha gene may be an important mechanism by which mutations in the hedgehog pathway cause BCCs. Animal model experiments lend further support to the function of PDGFRA. Klinghoffer et al. (2001) created 2 complementary lines of knockin mice in which the intracellular signaling domains of one PDGFR had been removed and replaced by those of the other PDGFR. While both lines demonstrated substantial rescue of normal development, substitution of the *Pdgfrb* signaling domains with those of *Pdgfra* resulted in varying degrees of vascular disease.

[9588] It is appreciated that the abovementioned animal model for PDGFRA is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further ap-

preciated from the publications sited hereinbelow.

[9589] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9590] Xie, J.; Aszterbaum, M.; Zhang, X.; Bonifas, J. M.; Zachary, C.; Epstein, E.; McCormick, F. : A role of PDGFR-alpha in basal cell carcinoma proliferation. Proc. Nat. Acad. Sci. 98: 9255-9259, 2001. ; and

[9591] Klinghoffer, R. A.; Muetting-Nelsen, P. F.; Faerman, A.; Shani, M.; Soriano, P. : The two PDGF receptors maintain conserved signaling in vivo despite divergent embryological functions.

[9592] Further studies establishing the function and utilities of PDGFRA are found in John Hopkins OMIM database record ID 173490, and in sited publications numbered 12457-12458, 10725, 12459-12462, 12641, 353 and 3535-1207 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0222 (Accession NM_014643) is another VGAM117 host target gene. KIAA0222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0222, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0222 BINDING SITE, designated SEQ ID:16047, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, also designated SEQ ID:2828.

[9593] Another function of VGAM117 is therefore inhibition of KIAA0222 (Accession NM_014643). Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0222. PRO1600 (Accession NM_014095) is another VGAM117 host target gene. PRO1600 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1600 BINDING SITE, designated SEQ ID:15315, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, also designated SEQ ID:2828.

[9594] Another function of VGAM117 is therefore inhibition of PRO1600 (Accession NM_014095). Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1600.

TEB4 (Accession XM_027156) is another VGAM117 host target gene. TEB4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TEB4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEB4 BINDING SITE, designated SEQ ID:30429, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, also designated SEQ ID:2828.

[9595] Another function of VGAM117 is therefore inhibition of TEB4 (Accession XM_027156). Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEB4. LOC125268 (Accession XM_071960) is another VGAM117 host target gene. LOC125268 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC125268, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125268 BINDING SITE, designated SEQ ID:37452, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA,

also designated SEQ ID:2828.

[9596] Another function of VGAM117 is therefore inhibition of LOC125268 (Accession XM_071960). Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC125268. LOC220469 (Accession XM_084334) is another VGAM117 host target gene. LOC220469 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220469 BINDING SITE, designated SEQ ID:37556, to the nucleotide sequence of VGAM117 RNA, herein designated VGAM RNA, also designated SEQ ID:2828.

[9597] Another function of VGAM117 is therefore inhibition of LOC220469 (Accession XM_084334). Accordingly, utilities of VGAM117 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220469. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 118 (VGAM118) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9598] VGAM118 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM118 was detected is described hereinabove with reference to Figs. 1–8.

[9599] VGAM118 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9600] VGAM118 gene encodes a VGAM118 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM118 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM118 precursor RNA is designated SEQ ID:104, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:104 is located at position 178358 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9601] VGAM118 precursor RNA folds onto itself, forming VGAM118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9602] An enzyme complex designated DICER COMPLEX, `dices` the VGAM118 folded precursor RNA into VGAM118 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM118 RNA is designated SEQ ID:2829, and is provided hereinbelow with reference to the sequence listing part.

[9603] VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM118 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM118 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9604] VGAM118 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM118 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM118 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9605] The complementary binding of VGAM118 RNA, herein designated VGAM RNA, to host target binding sites on VGAM118 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM118 host target RNA into VGAM118 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9606] It is appreciated that VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM118 host target genes. The mRNA of each one of this plurality of VGAM118 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM118 RNA, herein designated VGAM RNA, and which when bound by VGAM118 RNA causes inhibition of translation of respective one or more VGAM118 host target proteins.

[9607] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM118 gene, herein designated VGAM GENE, on one or more VGAM118 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9608] It is yet further appreciated that a function of VGAM118 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM118 correlate

with, and may be deduced from, the identity of the host target genes which VGAM118 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9609] Nucleotide sequences of the VGAM118 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM118 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM118 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM118 are further described hereinbelow with reference to Table 1.

[9610] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM118 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM118 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9611] As mentioned hereinabove with reference to Fig. 1, a function of VGAM118 gene, herein designated VGAM is inhibition of expression of VGAM118 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM118 correlate with, and may be deduced

from, the identity of the target genes which VGAM118 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9612] Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199) is a VGAM118 host target gene. EIF2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C1 BINDING SITE, designated SEQ ID:14507, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9613] A function of VGAM118 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199), a gene which plays an important role in the eukaryotic peptide chain initiation process. Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2C1. The function of EIF2C1 has been established by previous studies. Koesters et al. (1999) isolated a EIF2C1 cDNA from a human fetal kidney cDNA library. To

obtain genomic sequence information, they isolated a P1 genomic clone containing the EIF2C1 locus. The human EIF2C1 gene encodes a protein of 857 amino acids. The 2,571-bp open reading frame is flanked by 238 bp of 5-prime sequence and an extremely large 3-prime untranslated region with multiple short repeated segments composed of mono-, tri-, or quatrunucleotides interspersed throughout. Northern blot analysis demonstrated that the human EIF2C1 gene is ubiquitously expressed at low to medium levels. Differential polyadenylation and splicing resulted in a complex transcriptional pattern. Martinez et al. (2002) demonstrated that a single-stranded small interfering RNA (siRNA) resides in the human RNA-induced silencing complex (RISC) together with the EIF2C1 and/or EIF2C2 (OMIM Ref. No. 606229) proteins. RISC could be rapidly formed in HeLa cell cytoplasmic extract supplemented with 21-nucleotide siRNA duplexes, but also by adding single-stranded antisense RNAs, which range in size between 19 and 29 nucleotides.

[9614] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9615] Koesters, R.; Adams, V.; Betts, D.; Moos, R.; Schmid, M.;

Siermann, A.; Hassam, S.; Weitz, S.; Lichter, P.; Heitz, P. U.; von Knebel Doeberitz, M.; Briner, J. : Human eukaryotic initiation factor EIF2C1 gene: cDNA sequence, genomic organization, localization to chromosomal bands 1q34–p35, and expression. Genomics 61: 210–218, 1999. ; and

[9616] Martinez, J.; Patkaniowska, A.; Urlaub, H.; Luhrmann, R.; Tusch, T. : Single-stranded antisense siRNAs guide target RNA cleavage in RNAi. Cell 110: 563–574, 2002.

[9617] Further studies establishing the function and utilities of EIF2C1 are found in John Hopkins OMIM database record ID 606228, and in cited publications numbered 6591–6592 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_000458) is another VGAM118 host target gene. TCF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE, designated SEQ ID:6075, to the nucleotide se-

quence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9618] Another function of VGAM118 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_000458), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 has been established by previous studies. Abbott et al. (1990) isolated and partially sequenced a human clone corresponding to the gene for liver-specific transcription factor LFB3. Furthermore, they designed oligonucleotide primers for TCF2 (also called HNF1B) and used them to amplify specifically the human gene in human/rodent somatic cell hybrids by the polymerase chain reaction. They showed that TCF2 maps to 17q between the centromere and the breakpoint of acute promyelocytic leukemia, i.e., proximal to 17q22. Hepatocyte nuclear factor-1 (HNF1A, or TCF1; 142410) is a homeodomain-containing transcriptional activator required for the liver-specific expression of a variety of genes. Bach et al. (1991) isolated a cDNA clone from a human liver library encoding a protein,

designated HNF1B, that is highly homologous to HNF1A (also called TCF1) in 3 regions, including the homeo domain and the dimerization domain. They showed that this protein can heterodimerize with human HNF1A in vitro. Sequence comparison with a rat variant HNF1A identified the cDNA as the human homolog. HNF1B is a nuclear protein recognizing the same binding site as HNF1A. By Northern blot analysis, Bach et al. (1991) showed that the HNF1B transcripts are present in differentiated human HepG2 hepatoma cells as well as in rat liver and that this transcript level is 10- to 20-fold lower than that of HNF1A. They assigned the HNF1B gene to human chromosome 17 and mouse chromosome 11. The HNF1A gene maps to human chromosome 12 and mouse chromosome 5.

[9619] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9620] Abbott, C.; Piaggio, G.; Ammendola, R.; Solomon, E.; Povey, S.; Gounari, F.; De Simone, V.; Cortese, R. : Mapping of the gene TCF2 for the transcription factor LFB3 to human chromosome 17 by polymerase chain reaction. Genomics 8: 165-167, 1990. ; and

- [9621] Bach, I.; Mattei, M.-G.; Cereghini, S.; Yaniv, M. : Two members of an HNF1 homeoprotein family are expressed in human liver. *Nucleic Acids Res.* 19: 3553–3559, 1991.
- [9622] Further studies establishing the function and utilities of TCF2 are found in John Hopkins OMIM database record ID 189907, and in cited publications numbered 12603–12604, 2181, 12605–12606, 2182, 2529, 12607–12608, 218 and 12609 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin M4 (CNNM4, Accession NM_020184) is another VGAM118 host target gene. CNNM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM4 BINDING SITE, designated SEQ ID:21425, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.
- [9623] Another function of VGAM118 is therefore inhibition of Cyclin M4 (CNNM4, Accession NM_020184). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with CNM4. Histamine Receptor H4 (HRH4, Accession NM_021624) is another VGAM118 host target gene. HRH4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH4 BINDING SITE, designated SEQ ID:22261, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9624] Another function of VGAM118 is therefore inhibition of Histamine Receptor H4 (HRH4, Accession NM_021624). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH4. KIAA1449 (Accession NM_020839) is another VGAM118 host target gene. KIAA1449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1449 BINDING SITE, designated SEQ ID:21897, to the nucleotide sequence of VGAM118 RNA, herein designated

VGAM RNA, also designated SEQ ID:2829.

[9625] Another function of VGAM118 is therefore inhibition of KIAA1449 (Accession NM_020839). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1449. KIAA1981 (Accession XM_114000) is another VGAM118 host target gene. KIAA1981 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1981 BINDING SITE, designated SEQ ID:42609, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9626] Another function of VGAM118 is therefore inhibition of KIAA1981 (Accession XM_114000). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1981. Rho-related BTB Domain Containing 3 (RHOBTB3, Accession NM_014899) is another VGAM118 host target gene. RHOBTB3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by RHOBTB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB3 BINDING SITE, designated SEQ ID:17078, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9627] Another function of VGAM118 is therefore inhibition of Rho-related BTB Domain Containing 3 (RHOBTB3, Accession NM_014899). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB3. LOC149076 (Accession XM_086415) is another VGAM118 host target gene. LOC149076 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149076, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149076 BINDING SITE, designated SEQ ID:38639, to the nucleotide sequence of VGAM118 RNA, herein designated VGAM RNA, also designated SEQ ID:2829.

[9628] Another function of VGAM118 is therefore inhibition of

LOC149076 (Accession XM_086415). Accordingly, utilities of VGAM118 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149076. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 119 (VGAM119) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9629] VGAM119 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM119 was detected is described hereinabove with reference to Figs. 1–8.

[9630] VGAM119 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9631] VGAM119 gene encodes a VGAM119 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM119 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM119 precursor RNA is designated SEQ ID:105, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:105 is located at position 278814 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9632] VGAM119 precursor RNA folds onto itself, forming VGAM119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9633] An enzyme complex designated DICER COMPLEX, `dices` the VGAM119 folded precursor RNA into VGAM119 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 41%) nucleotide sequence of VGAM119 RNA is designated SEQ ID:2830, and is provided hereinbelow with reference to the sequence listing part.

[9634] VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM119 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[9635] VGAM119 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM119 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM119 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9636] The complementary binding of VGAM119 RNA, herein designated VGAM RNA, to host target binding sites on VGAM119 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM119 host target RNA into VGAM119 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9637] It is appreciated that VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM119 host target genes. The mRNA of each one of this plurality of VGAM119 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM119 RNA, herein designated VGAM RNA, and which when bound by VGAM119 RNA causes inhibition of translation of respective one or more VGAM119 host target proteins.

[9638] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM119 gene, herein designated VGAM GENE, on one or more VGAM119 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9639] It is yet further appreciated that a function of VGAM119 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM119 correlate with, and may be deduced from, the identity of the host target genes which VGAM119 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9640] Nucleotide sequences of the VGAM119 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM119 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM119 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM119 are further described hereinbelow with reference to Table 1.

[9641] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM119 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM119 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[9642] As mentioned hereinabove with reference to Fig. 1, a function of VGAM119 gene, herein designated VGAM is inhibition of expression of VGAM119 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM119 correlate with, and may be deduced from, the identity of the target genes which VGAM119 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9643] Phospholamban (PLN, Accession NM_002667) is a VGAM119 host target gene. PLN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLN BINDING SITE, designated SEQ ID:8538, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9644] A function of VGAM119 is therefore inhibition of Phospholamban (PLN, Accession NM_002667), a gene which regulates the activity of the calcium pump of cardiac sar-

coplasmic reticulum. Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLN. The function of PLN has been established by previous studies. Fujii et al. (1991) isolated and characterized genomic DNA clones encoding rabbit phospholamban. The phospholamban gene of 13.2 kb contained only one 10.5-kb intron which separated exonic sequences located in the 5-prime untranslated region. Phospholamban, through modulation of sarcoplasmic reticulum calcium-ATPase activity, is a key regulator of cardiac diastolic function. Alterations in phospholamban expression may define parameters of muscle relaxation. McTiernan et al. (1999) observed that human ventricle and quadriceps displayed high levels of phospholamban transcripts and proteins, with markedly lower expression observed in smooth muscles, while the right atrium also expressed low levels of phospholamban. The structure of the human phospholamban gene closely resembles that reported for chicken, rabbit, rat, and mouse. Comparison of the human to other mammalian phospholamban genes indicated a marked conservation of sequence for at least 217 bp upstream of the transcription start site.

- [9645] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9646] Fujii, J.; Zarain-Herzberg, A.; Willard, H. F.; Tada, M.; MacLennan, D. H. : Structure of the rabbit phospholamban gene, cloning of the human cDNA, and assignment of the gene to human chromosome 6. J. Biol. Chem. 266: 11669–11675, 1991. ; and
- [9647] McTiernan, C. F.; Frye, C. S.; Lemster, B. H.; Kinder, E. A.; Ogletree-Hughes, M. L.; Moravec, C. S.; Feldman, A. M. : The human phospholamban gene: structure and expression. J. Molec. Cell.
- [9648] Further studies establishing the function and utilities of PLN are found in John Hopkins OMIM database record ID 172405, and in cited publications numbered 10832–10834 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SMT3 Suppressor of Mif Two 3 Homolog 1 (yeast) (SMT3H1, Accession XM_009805) is another VGAM119 host target gene. SMT3H1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMT3H1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMT3H1 BINDING SITE, designated SEQ ID:30125, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9649] Another function of VGAM119 is therefore inhibition of SMT3 Suppressor of Mif Two 3 Homolog 1 (yeast) (SMT3H1, Accession XM_009805), a gene which is involved in the function and/or structure of the eukaryotic kinetochore. Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMT3H1. The function of SMT3H1 has been established by previous studies. TEXT Lapenta et al. (1997) used cDNA selection to isolate coding sequences from cosmids mapping to the gene-rich telomeric region of human chromosome 21q. A cDNA, which the authors termed SMT3A, was isolated and mapped between the loci PFKL and D21S171 on 21q22.3, about 2.2 Mb proximal to the telomere. The predicted protein of 103 amino acids was found to be a homolog of the *S. cerevisiae* SMT3 protein, whose gene was previously isolated as a suppressor of mutations in the MIF2 gene (Meluh and Koshland, 1995). The yeast MIF2 gene en-

codes an essential centromeric protein and shows homology to mammalian CENPC (see OMIM Ref. No. 117141), an integral component of active kinetochores (Meluh and Koshland, 1995). The proposed role of yeast SMT3 as a centromeric protein and the strong evolutionary conservation of the human SMT3A gene suggested to Lapenta et al. (1997) that the encoded protein is involved in the function and/or structure of the eukaryotic kinetochore. SMT3A is also highly homologous to ubiquitin (OMIM Ref. No. 191320). Lapenta et al. (1997) identified 2 additional human SMT3-like sequences, named SMT3B (OMIM Ref. No. 603042) and SMT3C (OMIM Ref. No. 601912), as expressed sequence tags; SMT3A shares 87% amino acid identity with SMT3B and 47% identity with SMT3C.

[9650] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9651] Lapenta, V.; Chiurazzi, P.; van der Spek, P.; Pizzuti, A.; Hanaoka, F.; Brahe, C. : SMT3A, a human homologue of the *S. cerevisiae* SMT3 gene, maps to chromosome 21qter and defines a novel gene family. *Genomics* 40: 362–366, 1997. ; and

[9652] Meluh, P. B.; Koshland, D. : Suppressors of MIF2, a puta-

tive centromere protein gene in *Saccharomyces cerevisiae*.
(Abstract) *Molec. Biol. Cell* 6 (supp.): 360a only, 1995.

[9653] Further studies establishing the function and utilities of SMT3H1 are found in John Hopkins OMIM database record ID 602231, and in cited publications numbered 9136–6288 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. EZFIT (Accession NM_021216) is another VGAM119 host target gene. EZFIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZFIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EZFIT BINDING SITE, designated SEQ ID:22195, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9654] Another function of VGAM119 is therefore inhibition of EZFIT (Accession NM_021216). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZFIT. FLJ13110 (Accession NM_022912) is another VGAM119 host target gene. FLJ13110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ13110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13110 BINDING SITE, designated SEQ ID:23223, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9655] Another function of VGAM119 is therefore inhibition of FLJ13110 (Accession NM_022912). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13110. KIAA0429 (Accession NM_014751) is another VGAM119 host target gene. KIAA0429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0429 BINDING SITE, designated SEQ ID:16475, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9656] Another function of VGAM119 is therefore inhibition of KIAA0429 (Accession NM_014751). Accordingly, utilities

of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0429. KIAA0662 (Accession XM_088539) is another VGAM119 host target gene. KIAA0662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0662 BINDING SITE, designated SEQ ID:39802, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9657] Another function of VGAM119 is therefore inhibition of KIAA0662 (Accession XM_088539). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0662. KIAA1371 (Accession XM_114371) is another VGAM119 host target gene. KIAA1371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1371 BINDING SITE, designated SEQ ID:42907, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9658] Another function of VGAM119 is therefore inhibition of KIAA1371 (Accession XM_114371). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1371. KIAA1508 (Accession XM_030209) is another VGAM119 host target gene. KIAA1508 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1508 BINDING SITE, designated SEQ ID:30993, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9659] Another function of VGAM119 is therefore inhibition of KIAA1508 (Accession XM_030209). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1508. moblak (Accession NM_130807) is another VGAM119 host target gene. moblak BINDING SITE is HOST

TARGET binding site found in the 5` untranslated region of mRNA encoded by moblak, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of moblak BINDING SITE, designated SEQ ID:28310, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9660] Another function of VGAM119 is therefore inhibition of moblak (Accession NM_130807). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with moblak. RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM_032144) is another VGAM119 host target gene. RAB6C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAB6C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6C BINDING SITE, designated SEQ ID:25836, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9661] Another function of VGAM119 is therefore inhibition of RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM_032144). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6C. LOC219899 (Accession XM_166173) is another VGAM119 host target gene. LOC219899 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219899, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219899 BINDING SITE, designated SEQ ID:43990, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9662] Another function of VGAM119 is therefore inhibition of LOC221773 (Accession XM_165802). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221773. LOC221773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221773, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221773 BINDING SITE, designated SEQ ID:43762, to the nucleotide sequence of VGAM119 RNA, herein designated VGAM RNA, also designated SEQ ID:2830.

[9663] Another function of VGAM119 is therefore inhibition of LOC221773 (Accession XM_165802). Accordingly, utilities of VGAM119 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221773. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 120 (VGAM120) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9664] VGAM120 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM120 was detected is described hereinabove with reference to Figs. 1–8.

[9665] VGAM120 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syn–

drome Virus (white spot bacilliform virus). VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9666] VGAM120 gene encodes a VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM120 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM120 precursor RNA is designated SEQ ID:106, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:106 is located at position 277493 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9667] VGAM120 precursor RNA folds onto itself, forming VGAM120 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9668] An enzyme complex designated DICER COMPLEX, `dices` the VGAM120 folded precursor RNA into VGAM120 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM120 RNA is designated SEQ ID:2831, and is provided hereinbelow with reference to the sequence listing part.

[9669] VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM120 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9670] VGAM120 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM120 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM120 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9671] The complementary binding of VGAM120 RNA, herein designated VGAM RNA, to host target binding sites on VGAM120 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM120 host tar–

get RNA into VGAM120 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9672] It is appreciated that VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM120 host target genes. The mRNA of each one of this plurality of VGAM120 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM120 RNA, herein designated VGAM RNA, and which when bound by VGAM120 RNA causes inhibition of translation of respective one or more VGAM120 host target proteins.

[9673] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM120 gene, herein designated VGAM GENE, on one or more VGAM120 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9674] It is yet further appreciated that a function of VGAM120 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM120 correlate with, and may be deduced from, the identity of the host target genes which VGAM120 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9675] Nucleotide sequences of the VGAM120 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM120 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM120 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM120 are further described hereinbelow with reference to Table 1.

[9676] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM120 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM120 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9677] As mentioned hereinabove with reference to Fig. 1, a function of VGAM120 gene, herein designated VGAM is inhibition of expression of VGAM120 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM120 correlate with, and may be deduced from, the identity of the target genes which VGAM120 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9678] Adenylate Cyclase 2 (brain) (ADCY2, Accession XM_036383) is a VGAM120 host target gene. ADCY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of ADCY2 BINDING SITE, designated SEQ ID:32436, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9679] A function of VGAM120 is therefore inhibition of Adenylate Cyclase 2 (brain) (ADCY2, Accession XM_036383), a gene which Adenylate cyclase (type 2), an ATP-pyrophosphate lyase; converts ATP to cAMP. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY2. The function of ADCY2 has been established by previous studies. Stengel et al. (1992) identified a brain cDNA corresponding to a gene that encodes a human brain adenylyl cyclase, which they symbolized HBAC2. The amino acid sequence of ADCY2 displayed significant homology with ADCY8 (OMIM Ref. No. 103070) in the highly conserved adenylyl cyclase domain (250 amino acids) found in the 3-prime cytoplasmic portion of all mammalian adenylyl cyclases. However, outside this domain, the homology was extremely low. By in situ hybridization to metaphase chromosomal spreads using a human brain cDNA probe, they demonstrated that the ADCY2 gene maps to 5p15.3. There was no cross-reactivity with the

site on 8q24.2 where ADCY8 was found to map. Using Southern blot analysis of somatic cell hybrid DNAs, Gaudin et al. (1994) likewise mapped type II adenylyl cyclase to chromosome 5. Furthermore, they determined the chromosomal location of 4 other isoforms: type III on chromosome 2, type IV on chromosome 14, type V on chromosome 3, and type VI on chromosome 12. By fluorescence in situ hybridization, Edelhoff et al. (1995) mapped the mouse homolog to chromosome 13 in the C1 region. Wong et al. (2000) identified the presence of adenylyl cyclases 2, 3 (OMIM Ref. No. 600291), and 4 (OMIM Ref. No. 600292) in olfactory cilia.

[9680] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9681] Edelhoff, S.; Villacres, E. C.; Storm, D. R.; Disteché, C. M. : Mapping of adenylyl cyclase genes type I, II, III, IV, V, and VI in mouse. *Mammalian Genome* 6: 111–113, 1995. ; and

[9682] Wong, S. T.; Trinh, K.; Hacker, B.; Chan, G. C. K.; Lowe, G.; Gaggari, A.; Xia, Z.; Gold, G. H.; Storm, D. R. : Disruption of the type III adenylyl cyclase gene leads to peripheral and be.

[9683] Further studies establishing the function and utilities of

ADCY2 are found in John Hopkins OMIM database record ID 103071, and in cited publications numbered 494–495, 49 and 496 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Alpha-methylacyl-CoA Racemase (AMACR, Accession XM_043771) is another VGAM120 host target gene. AMACR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AMACR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMACR BINDING SITE, designated SEQ ID:34015, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9684] Another function of VGAM120 is therefore inhibition of Alpha-methylacyl-CoA Racemase (AMACR, Accession XM_043771). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMACR. Caspase 6, Apoptosis-related Cysteine Protease (CASP6, Accession NM_032992) is another VGAM120 host target gene. CASP6 BINDING SITE1 and CASP6 BINDING SITE2 are HOST

TARGET binding sites found in untranslated regions of mRNA encoded by CASP6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP6 BINDING SITE1 and CASP6 BINDING SITE2, designated SEQ ID:26873 and SEQ ID:6894 respectively, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9685] Another function of VGAM120 is therefore inhibition of Caspase 6, Apoptosis-related Cysteine Protease (CASP6, Accession NM_032992), a gene which involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP6. The function of CASP6 has been established by previous studies. Fernandes-Alnemri et al. (1995) isolated MCH2, a member of the ced-3 subfamily of apoptotic proteases, by performing PCR on human Jurkat T lymphocytes using degenerate oligonucleotides corresponding to conserved peptides in known apoptotic cysteine proteases. The gene, also symbolized CASP6, encodes a 34-kD protein that is highly homolo-

gous to human CPP32 (OMIM Ref. No. 600636), *C. elegans* ced-3, mammalian Ich1/Nedd2 (OMIM Ref. No. 600639), and mammalian interleukin-1-beta converting enzyme (OMIM Ref. No. 147678). Fernandes-Alnemri et al. (1995) observed 1.7-kb (alpha) and 1.4-kb (beta) transcripts expressed in Jurkat lymphocytes and other cell lines. The authors suggested that these transcripts are alternate splicing variants and found that the alpha, but not the beta, MCH2 protein has protease activity. They also found that MCH2-alpha protein can cleave poly(ADP-ribose) polymerase (OMIM Ref. No. 173870) in vitro and that its overexpression induces apoptosis in insect Sf9 cells, suggesting that MCH2 is a mediator of apoptosis in mammalian cells. Using protease assays and immunoblotting experiments, Orth et al. (1996) showed that MCH2, like CPP32 and MCH3, functions downstream of the mammalian cell death inhibitors Bcl2 (OMIM Ref. No. 151430) and BclXL and of the viral serpin CrmA. Further, they found that granzyme B can functionally activate MCH2, supporting the idea that granzyme B kills cells by activating downstream components of the CED-3/ICE apoptotic pathway. Orth et al. (1996) also showed that MCH2, unlike CPP32 and MCH3, can cleave lamin A to its signature

apoptotic fragment.

[9686] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9687] Fernandes-Alnemri, T.; Litwack, G.; Alnemri, E. S. : Mch2, a new member of the apoptotic Ced-3/Ice cysteine protease gene family. Cancer Res. 55: 2737-2742, 1995. ; and

[9688] Orth, K.; Chinnaiyan, A. M.; Garg, M.; Froelich, C. J.; Dixit, V. M. : The CED-3/ICE-like protease Mch2 is activated during apoptosis and cleaves the death substrate lamin A. J. Biol. Ch.

[9689] Further studies establishing the function and utilities of CASP6 are found in John Hopkins OMIM database record ID 601532, and in cited publications numbered 7200, 720 and 7202 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1) (GALNT1, Accession NM_020474) is another VGAM120 host target gene. GALNT1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GALNT1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT1 BINDING SITE, designated SEQ ID:21724, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9690] Another function of VGAM120 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1) (GALNT1, Accession NM_020474), a gene which transfers an N-acetyl galactosamine (GalNAc) to a serine or threonine residue in the first step of O-linked oligosaccharide biosynthesis. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT1. The function of GALNT1 has been established by previous studies. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase (GalNAc-T; EC 2.4.1.41) transfers an N-acetyl galactosamine (OMIM Ref. No. GalNAc) to a serine or threonine residue in the first step of O-linked oligosaccharide biosynthesis. Takai et al. (1997) cloned the GALNT1 gene, termed GalNAc-T1 by them, from human colon tissue, using a reverse transcriptase

polymerase chain reaction (OMIM Ref. No. RT-PCR) with oligonucleotide primers based on the nucleotide sequence of bovine GalNAc-T1 cDNA. The predicted GALNT1 protein is 559 amino acids long and has 99.6% sequence similarity with the bovine protein. White et al. (1995) isolated cDNAs encoding human GalNAc-T1 and GalNAc-T2 (GALNT2; 602274). Bennett et al. (1998) found that the GALNT1, GALNT2, and GALNT3 (OMIM Ref. No. 601756) genes contain 11, 16, and 10 exons, respectively. Several intron/exon boundaries were conserved within the 3 genes. By fluorescence in situ hybridization, Takai et al. (1997) mapped the GALNT1 gene to chromosome 18q12.1. By the same method, Bennett et al. (1998) mapped the gene to 18q12-q21.

[9691] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9692] Bennett, E. P.; Weghuis, D. O.; Merkx, G.; Geurts van Kessel, A.; Eiberg, H.; Clausen, H. : Genomic organization and chromosomal localization of three members of the UDP-N-acetylgalactosamine:polypeptide N-acetylgalactosaminyltransferase family. *Glycobiology* 8: 547-555, 1998. ; and

- [9693] Takai, S.; Hinoda, Y.; Adachi, T.; Imai, K.; Oshima, M. : A human UPD (sic)-GalNAc: polypeptide, N-acetylgalactosaminyltransferase type 1 gene is located at the chromosomal region 18q12.
- [9694] Further studies establishing the function and utilities of GALNT1 are found in John Hopkins OMIM database record ID 602273, and in cited publications numbered 2824-2798 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450) is another VGAM120 host target gene. KLHL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL3 BINDING SITE, designated SEQ ID:42272, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.
- [9695] Another function of VGAM120 is therefore inhibition of Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with KLHL3. Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694) is another VGAM120 host target gene. PKHD1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PKHD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKHD1 BINDING SITE, designated SEQ ID:28944, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9696] Another function of VGAM120 is therefore inhibition of Polycystic Kidney and Hepatic Disease 1 (autosomal recessive) (PKHD1, Accession NM_138694). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKHD1. Pinin, Desmosome Associated Protein (PNN, Accession XM_048719) is another VGAM120 host target gene. PNN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PNN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PNN BINDING SITE, designated SEQ ID:35234, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9697] Another function of VGAM120 is therefore inhibition of Pinin, Desmosome Associated Protein (PNN, Accession XM_048719), a gene which reinforces the intermediate filament–desmosome complex. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNN. The function of PNN has been established by previous studies. Desmosomes are intimately involved in the structural and functional integration of adjacent epithelial cells. They serve as reinforcement sites of cell–cell adhesion, as well as points for lateral anchorage of the intermediate scaffold of the epithelial cell. A number of proteins associated with desmosomes have been identified, including desmoplakin (OMIM Ref. No. 125647), plakoglobin (OMIM Ref. No. 173325), desmogleins (e.g., 125670), and desmocollins (e.g., 125643). Ouyang and Sugrue (1996) identified a novel phosphoprotein, called pinin, that associates with mature desmosomes. By screening a human placenta cDNA library with a canine pinin cDNA cloned by them,

they isolated cDNAs encoding PNN. The deduced 743-amino acid PNN protein contains a serine-rich domain; a glutamine-proline, glutamine-leucine repeat domain; an acidic domain rich in glutamic acid; and numerous potential kinase recognition motifs. Recombinant PNN migrated as a 140-kD protein by Western blot analysis. Ouyang and Sugrue (1996) found that recombinant pinin was expressed along the lateral borders of human embryonic kidney-derived 293 cells, in association with desmoplakin; they noted striking changes in cell/tissue morphology. Northern blot analysis detected ubiquitous expression of PNN in human tissues, including those lacking desmosomes. PNN is expressed as 4.1-, 3.7-, and 3.2-kb transcripts that show tissue-specific expression patterns. Southern blot analysis demonstrated the existence of a single pinin gene in the human genome. Since the 3-prime end of the PNN coding sequence is nearly identical to a partial cDNA identified in a pig neutrophil cDNA library, and since leukocytes, which do not react with antibodies against pinin, express an mRNA that hybridizes with a pinin cDNA, the authors speculated that there may be a pinin-related gene. By screening a keratinocyte cDNA library, Brandner et al. (1997) and Brandner et al. (1998)

isolated a cDNA encoding a protein, which they called DRS (domain rich in serine), that is essentially identical to the PNN protein described by Ouyang and Sugrue (1996).

However, cell fractionation and immunofluorescence microscopy analysis localized DRS strictly to the nucleus and not to desmosomes. Sequence analysis predicted that the 717-amino acid DRS protein contains an N-terminal nuclear localization signal and a C-terminal stretch of approximately 80 amino acids, 73% of which are serine. The 80-amino acid C-terminal domain and a subsequent 79-amino acid domain also contain numerous ser-arg and arg-ser dipeptides.

[9698] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9699] Ouyang, P.; Sugrue, S. P. : Characterization of pinin, a novel protein associated with the desmosome-intermediate filament complex. *J. Cell Biol.* 135: 1027-1042, 1996.
; and

[9700] Brandner, J. M.; Reidenbach, S.; Kuhn, C.; Franke, W. W. : Identification and characterization of a novel kind of nuclear protein occurring free in nucleoplasm and in ribonucleoprotein st.

[9701] Further studies establishing the function and utilities of PNN are found in John Hopkins OMIM database record ID 603154, and in cited publications numbered 2423–2426 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Palmitoyl–protein Thioesterase 2 (PPT2, Accession NM_138717) is another VGAM120 host target gene. PPT2 BINDING SITE1 and PPT2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPT2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPT2 BINDING SITE1 and PPT2 BINDING SITE2, designated SEQ ID:28964 and SEQ ID:11633 respectively, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9702] Another function of VGAM120 is therefore inhibition of Palmitoyl–protein Thioesterase 2 (PPT2, Accession NM_138717), a gene which is a palmitoyl–protein thioesterase 2 which possesses a different substrate specificity than PPT1. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPT2. The function

of PPT2 has been established by previous studies. Palmitoyl-protein thioesterase-1 (PPT1; 600722) is a lysosomal hydrolase that removes long-chain fatty acyl groups from modified cysteine residues in proteins. Mutations in PPT1 have been found to cause the infantile form of neuronal ceroid lipofuscinosis (INCL; 256730). By searching sequence databases for homologs of PPT1, Soyombo and Hofmann (1997) identified cDNAs encoding PPT2. The deduced PPT2 protein contains 302 amino acids, including a 27-amino acid leader peptide, a sequence motif characteristic of many thioesterases and lipases, and 5 potential N-linked glycosylation sites. PPT2 shares 18% amino acid identity with PPT1. Northern blot analysis detected a predominant 2.0-kb PPT2 transcript in the human tissues examined, with the highest expression in skeletal muscle; variable amounts of 2.8- and 7.0-kb transcripts were also observed. Immunoblot analysis of recombinant PPT2 expressed in mammalian cells showed 6 PPT2 proteins ranging in size from 31 to 42 kD. Treatment that removes asparagine-linked oligosaccharides resulted in a single major protein of 31 kD and a minor protein of 33 kD. The authors demonstrated that recombinant PPT2, like PPT1, possesses thioesterase activity and localizes to the lyso-

some. Since PPT2 could not substitute for PPT1 in correcting the metabolic defect in INCL cells and was unable to remove palmitate groups from palmitoylated proteins that are routinely used as substrates for PPT1, Soyombo and Hofmann (1997) suggested that PPT2 possesses a different substrate specificity than PPT1. Animal model experiments lend further support to the function of PPT2. Gupta et al. (2001) engineered disruptions in the Ppt1 and Ppt2 genes to create knockout mice that were deficient in either enzyme. Both lines of mice were viable and fertile; however, both lines developed spasticity (a 'claspings' phenotype) at a median age of 21 weeks and 29 weeks, respectively. Motor abnormalities progressed in the Ppt1 knockout mice, leading to death by 10 months of age. In contrast, most Ppt2 mice were alive at 12 months. Myoclonic jerking and seizures were prominent in the Ppt1 mice. Autofluorescent storage material was striking throughout the brains of both strains of mice. Neuronal loss and apoptosis were particularly prominent in Ppt1-deficient brains. These studies provided a mouse model for infantile neuronal ceroid lipofuscinosis and further suggested that PPT2 serves a role in the brain that is not carried out by PPT1.

[9703] It is appreciated that the abovementioned animal model for PPT2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9704] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9705] Gupta, P.; Soyombo, A. A.; Atashband, A.; Wisniewski, K. E.; Shelton, J. M.; Richardson, J. A.; Hammer, R. E.; Hofmann, S. L. : Disruption of PPT1 or PPT2 causes neuronal ceroid lipofuscinosis in knockout mice. Proc. Nat. Acad. Sci. 98: 13566–13571, 2001. ; and

[9706] Soyombo, A. A.; Hofmann, S. L. : Molecular cloning and expression of palmitoyl–protein thioesterase 2 (PPT2), a homolog of lysosomal palmitoyl–protein thioesterase with a distinct subs.

[9707] Further studies establishing the function and utilities of PPT2 are found in John Hopkins OMIM database record ID 603298, and in cited publications numbered 6567 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Kinase, CAMP–dependent, Regulatory, Type II, Beta (PRKAR2B, Accession NM_002736) is another VGAM120 host target gene.

PRKAR2B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKAR2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKAR2B BINDING SITE, designated SEQ ID:8611, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9708] Another function of VGAM120 is therefore inhibition of Protein Kinase, CAMP-dependent, Regulatory, Type II, Beta (PRKAR2B, Accession NM_002736), a gene which type II regulatory chains mediate membrane association by binding to anchoring proteins, including the map2 kinase. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKAR2B. The function of PRKAR2B has been established by previous studies. Using both a rat skeletal muscle clone and a human clone of type II regulatory subunit of cyclic AMP-dependent protein kinase, Scambler et al. (1987) demonstrated that the human gene is located on chromosome 7, close to but separate from the cystic fibrosis locus (OMIM Ref. No. 219700). These conclusions

were based on Southern blot analysis of DNA from hybrid cell lines containing only chromosome 7 or parts thereof, as well as human/mouse hybrid cell lines established by means of chromosome-mediated gene transfer (CMGT) using MET (OMIM Ref. No. 164860) as a dominant selectable marker. Independence of PKR2 from CF was also indicated by family linkage studies using a RFLP of the PKR2 probe. Wainwright et al. (1987) showed that PKR2 is linked to several markers on 7q. The closest and strongest linkage was to TCRB (OMIM Ref. No. 186930), which showed a maximum lod score of 3.01 at $\theta = 0.00$. Using RFLPs in the CEPH panel of 40 families, Solberg et al. (1992) mapped the regulatory subunit RII-beta of cAMP-dependent protein kinase to 7q. They constructed a 7-point framework map including PRKAR2B and demonstrated the following order: cen--D7S371--(COL1A2, D7S79)--PRKAR2B--MET--D7S87--TCRB--qter. Furthermore, by in situ hybridization to metaphase chromosomes, Solberg et al. (1992) physically mapped PRKAR2B to 7q22. Cummings et al. (1996) generated knockout mice for the cyclic AMP dependent protein kinase regulatory subunit type II-beta (designated RII-beta by them). They reported that the mutants appeared healthy but had

markedly diminished white adipose tissue despite normal food intake and were protected against developing diet-induced obesity and fatty livers. In the mutant mice, brown adipose tissue demonstrated a compensatory increase in RI-alpha (OMIM Ref. No. 188830). Cummings et al. (1996) reported that RII-beta mutants exhibited markedly reduced leptin (OMIM Ref. No. 164160) mRNA and plasma levels; however, only mild hyperphagia was present

[9709] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9710] Cummings, D. E.; Brandon, E. P.; Planas, J. V.; Motamed, K.; Idzerda, R. L.; McKnight, G. S. : Genetically lean mice result from targeted disruption of the RII-beta subunit of protein kinase A. Nature 382: :622-626, 1996. ; and

[9711] Scambler, P.; Oyen, O.; Wainwright, B.; Farrall, M.; Law, H.-Y.; Estivill, X.; Sandberg, M.; Williamson, R.; Jahnsen, T. : Exclusion of catalytic and regulatory subunits of cAMP-dependen.

[9712] Further studies establishing the function and utilities of PRKAR2B are found in John Hopkins OMIM database record ID 176912, and in sited publications numbered

1157–1158, 115 and 1159 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB18, Member RAS Oncogene Family (RAB18, Accession NM_021252) is another VGAM120 host target gene. RAB18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB18 BINDING SITE, designated SEQ ID:22222, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9713] Another function of VGAM120 is therefore inhibition of RAB18, Member RAS Oncogene Family (RAB18, Accession NM_021252), a gene which plays a role in apical endocytosis/recycling. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB18. The function of RAB18 has been established by previous studies. Rab proteins are members of a family of Ras-related small GTPases that regulate membrane trafficking in organelles and transport vesicles. By stimulating umbilical vein en-

endothelial cells (HUVEC) with histamine and differential display gene expression analysis, Schafer et al. (2000) isolated a cDNA encoding RAB18. The deduced 206-amino acid protein shares 98%, 92%, and 85% identity with the mouse, snail, and worm sequences, respectively. RAB18 contains totally conserved phosphate/Mg(2+)-binding motifs and guanine-binding motifs as well as somewhat variable organelle-targeting regions. Northern blot analysis detected 2.5- and 1.0-kb transcripts in endothelial cells but not in smooth muscle cells or leukocytes. RT-PCR analysis suggested ubiquitous expression, which HPLC analysis determined to be strongest in heart, kidney, pancreas, lung, and liver, with weak expression in brain, placenta, and skeletal muscle. Stimulation of polarized HUVEC or nonpolarized mononuclear cells with histamine showed a significant time- and dose-dependent increase of RAB18 transcript in both cell types, suggesting a possible role for Rab proteins in inflammation. McMurtrie et al. (1997) mapped the mouse Rab18 gene to chromosome 18. They predicted that a human Rab18 homolog would map to 18q11-q12 or 10p11.

[9714] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [9715] McMurtrie, E. B.; Barbosa, M. D. F. S.; Zerial, M.; Kingsmore, S. F. : Rab17 and Rab18, small GTPases with specificity for polarized epithelial cells: genetic mapping in the mouse. *Genomics* 45: 623–625, 1997. ; and
- [9716] Schafer, U.; Seibold, S.; Schneider, A.; Neugebauer, E. : Isolation and characterisation of the human rab18 gene after stimulation of endothelial cells with histamine. *FEBS Lett.* 466: 1.
- [9717] Further studies establishing the function and utilities of RAB18 are found in John Hopkins OMIM database record ID 602207, and in cited publications numbered 8841–8842 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RecQ Protein-like 5 (RECQL5, Accession NM_004259) is another VGAM120 host target gene. RECQL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RECQL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RECQL5 BINDING SITE, designated SEQ ID:10451, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA,

also designated SEQ ID:2831.

[9718] Another function of VGAM120 is therefore inhibition of RecQ Protein-like 5 (RECQL5, Accession NM_004259). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RECQL5. Splicing Factor, Arginine/serine-rich 2 (SFRS2, Accession XM_036785) is another VGAM120 host target gene. SFRS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS2 BINDING SITE, designated SEQ ID:32505, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9719] Another function of VGAM120 is therefore inhibition of Splicing Factor, Arginine/serine-rich 2 (SFRS2, Accession XM_036785), a gene which is necessary for the splicing of pre-mrna. Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS2. The function of SFRS2 and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM47. Tripartite Motif-containing 34 (TRIM34, Accession NM_021616) is another VGAM120 host target gene. TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM34, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM34 BINDING SITE1 and TRIM34 BINDING SITE2, designated SEQ ID:22253 and SEQ ID:28177 respectively, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9720] Another function of VGAM120 is therefore inhibition of Tripartite Motif-containing 34 (TRIM34, Accession NM_021616). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM34. CSE-C (Accession XM_166163) is another VGAM120 host target gene. CSE-C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSE-C, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSE-C BINDING SITE, designated SEQ ID:43980, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9721] Another function of VGAM120 is therefore inhibition of CSE-C (Accession XM_166163). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSE-C. FLJ10482 (Accession NM_018107) is another VGAM120 host target gene. FLJ10482 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10482 BINDING SITE, designated SEQ ID:19876, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9722] Another function of VGAM120 is therefore inhibition of FLJ10482 (Accession NM_018107). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10482.

FLJ11149 (Accession NM_018339) is another VGAM120 host target gene. FLJ11149 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11149 BINDING SITE, designated SEQ ID:20346, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9723] Another function of VGAM120 is therefore inhibition of FLJ11149 (Accession NM_018339). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11149. FLJ11275 (Accession NM_018376) is another VGAM120 host target gene. FLJ11275 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11275 BINDING SITE, designated SEQ ID:20404, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2831.

[9724] Another function of VGAM120 is therefore inhibition of FLJ11275 (Accession NM_018376). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11275. FLJ14326 (Accession NM_032191) is another VGAM120 host target gene. FLJ14326 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14326 BINDING SITE, designated SEQ ID:25904, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9725] Another function of VGAM120 is therefore inhibition of FLJ14326 (Accession NM_032191). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14326. FLJ20527 (Accession NM_017863) is another VGAM120 host target gene. FLJ20527 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20527, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20527 BINDING SITE, designated SEQ ID:19540, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9726] Another function of VGAM120 is therefore inhibition of FLJ20527 (Accession NM_017863). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20527. KIAA1464 (Accession XM_043069) is another VGAM120 host target gene. KIAA1464 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1464 BINDING SITE, designated SEQ ID:33883, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9727] Another function of VGAM120 is therefore inhibition of KIAA1464 (Accession XM_043069). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1464. MGC13183 (Accession NM_032358) is another VGAM120 host target gene. MGC13183 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13183, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13183 BINDING SITE, designated SEQ ID:26146, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9728] Another function of VGAM120 is therefore inhibition of MGC13183 (Accession NM_032358). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13183. MGC16142 (Accession NM_032763) is another VGAM120 host target gene. MGC16142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC16142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16142 BINDING SITE, designated SEQ ID:26507, to

the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9729] Another function of VGAM120 is therefore inhibition of MGC16142 (Accession NM_032763). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16142. Wingless-type MMTV Integration Site Family, Member 2B (WNT2B, Accession NM_024494) is another VGAM120 host target gene. WNT2B BINDING SITE1 and WNT2B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT2B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT2B BINDING SITE1 and WNT2B BINDING SITE2, designated SEQ ID:23694 and SEQ ID:10393 respectively, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9730] Another function of VGAM120 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 2B (WNT2B, Accession NM_024494). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with WNT2B. LOC147622 (Accession XM_097255) is another VGAM120 host target gene. LOC147622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147622 BINDING SITE, designated SEQ ID:40851, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9731] Another function of VGAM120 is therefore inhibition of LOC147622 (Accession XM_097255). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147622. LOC150630 (Accession XM_097931) is another VGAM120 host target gene. LOC150630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150630 BINDING SITE, designated SEQ ID:41243, to

the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9732] Another function of VGAM120 is therefore inhibition of LOC150630 (Accession XM_097931). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150630. LOC155081 (Accession XM_088145) is another VGAM120 host target gene. LOC155081 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155081, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155081 BINDING SITE, designated SEQ ID:39546, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9733] Another function of VGAM120 is therefore inhibition of LOC155081 (Accession XM_088145). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155081. LOC196812 (Accession XM_116868) is another VGAM120 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43135, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9734] Another function of VGAM120 is therefore inhibition of LOC196812 (Accession XM_116868). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC221421 (Accession XM_166428) is another VGAM120 host target gene. LOC221421 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221421 BINDING SITE, designated SEQ ID:44326, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9735] Another function of VGAM120 is therefore inhibition of LOC221421 (Accession XM_166428). Accordingly, utilities

of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221421. LOC222228 (Accession XM_168627) is another VGAM120 host target gene. LOC222228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222228 BINDING SITE, designated SEQ ID:45277, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9736] Another function of VGAM120 is therefore inhibition of LOC222228 (Accession XM_168627). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222228. LOC222233 (Accession XM_168560) is another VGAM120 host target gene. LOC222233 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222233, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC222233 BINDING SITE, designated SEQ ID:45246, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9737] Another function of VGAM120 is therefore inhibition of LOC222233 (Accession XM_168560). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222233. LOC90906 (Accession XM_034809) is another VGAM120 host target gene. LOC90906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90906 BINDING SITE, designated SEQ ID:32152, to the nucleotide sequence of VGAM120 RNA, herein designated VGAM RNA, also designated SEQ ID:2831.

[9738] Another function of VGAM120 is therefore inhibition of LOC90906 (Accession XM_034809). Accordingly, utilities of VGAM120 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90906. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 121 (VGAM121) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9739] VGAM121 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM121 was detected is described hereinabove with reference to Figs. 1–8.

[9740] VGAM121 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9741] VGAM121 gene encodes a VGAM121 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM121 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM121 precursor RNA is designated SEQ ID:107, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:107 is located at position 104845 relative to the genome of

Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9742] VGAM121 precursor RNA folds onto itself, forming VGAM121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9743] An enzyme complex designated DICER COMPLEX, `dices` the VGAM121 folded precursor RNA into VGAM121 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM121 RNA is designated SEQ ID:2832, and is provided hereinbelow with reference to the sequence listing part.

[9744] VGAM121 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM121 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[9745] VGAM121 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM121 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM121 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM121 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[9746] The complementary binding of VGAM121 RNA, herein designated VGAM RNA, to host target binding sites on VGAM121 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM121 host target RNA into VGAM121 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9747] It is appreciated that VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM121 host target genes. The mRNA of each one of this plurality of VGAM121 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM121 RNA, herein designated VGAM RNA, and which when bound by VGAM121 RNA causes inhibition of translation of respective one or more VGAM121

host target proteins.

[9748] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM121 gene, herein designated VGAM GENE, on one or more VGAM121 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9749] It is yet further appreciated that a function of VGAM121 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syn-

drome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM121 correlate with, and may be deduced from, the identity of the host target genes which VGAM121 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9750] Nucleotide sequences of the VGAM121 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM121 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM121 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM121 are further described hereinbelow with reference to Table 1.

[9751] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM121 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM121 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9752] As mentioned hereinabove with reference to Fig. 1, a function of VGAM121 gene, herein designated VGAM is inhibition of expression of VGAM121 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM121 correlate with, and may be deduced from, the identity of the target genes which VGAM121 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9753] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 12 (CLECSF12, Accession XM_084768) is a VGAM121 host target gene.

CLECSF12 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLECSF12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF12 BINDING SITE, designated SEQ ID:37685, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9754] A function of VGAM121 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 12 (CLECSF12, Accession XM_084768), a gene which is a pattern-recognition receptor . Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with CLECSF12. The function of CLECSF12 has been established by previous studies. Yokota et al. (2001) cloned human dectin-1 using degenerative PCR amplification of mRNA isolated from dendritic cells and subsequent cDNA cloning. The human dectin-1 gene encodes a polypeptide of 247 amino acids, 3 amino acids longer than the mouse protein. Dectin-1 contains an immunoreceptor tyrosine-based activation motif within the cytoplasmic domain. Human dectin-1 mRNA is expressed predominantly in peripheral blood leukocytes and preferentially by dendritic cells. The mRNA encodes a 33-kD glycoprotein. In human epidermis, the protein is expressed selectively by Langerhans cells, which are an epidermal subset of dendritic cells. A truncated form of dectin-1 RNA encodes a polypeptide lacking almost the entire neck domain, which is required for accessibility of the carbohydrate recognition domain to ligands. Truncated dectin is produced by alternative splicing. Brown and Gordon (2001) identified dectin-1 as a beta-glucan receptor present on macrophages. In contrast to its reported specificity for dendritic cells (Yokota et al. (2001), Brown and Gordon (2001)) found that dectin-1 was expressed in every macrophage population examined and in

more tissues than was previously reported with the highest expression being in the liver, lung, and thymus. Brown and Gordon (2001) found that dectin-1 is a pattern-recognition receptor that recognizes a variety of beta-1,3-linked and beta-1,6-linked glucans from fungi and plants. Dectin-1 did not recognize monosaccharides or carbohydrates with different linkages. Laminarin and glucan phosphate, a structurally defined immunologically active beta-glucan, were the most effective inhibitors; both bind to the beta-glucan receptor on monocytes and macrophages. Soluble recombinant dectin-1 stimulates the proliferation of T lymphocytes (Ariizumi et al. (2000)). In a whole-cell binding assay, binding of T cells to NIH 3T3 cells expressing dectin-1 was not inhibited by beta-glucans. Therefore, Brown and Gordon (2001) concluded that dectin-1 has 2 ligand binding sites: one that recognizes an endogenous ligand on T cells, and another for exogenous carbohydrates.

[9755] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9756] Ariizumi, K.; Shen, G.-L.; Shikano, S.; Xu, S.; Ritter, R., III; Kumamoto, T.; Edelbaum, D.; Morita, A.; Bergstresser, P.

R.; Takashima, A. : Identification of a novel, dendritic cell-associated molecule, dectin-1, by subtractive cDNA cloning. J. Biol. Chem. 275: 20157-20167, 2000. ; and

[9757] Brown, G. D.; Gordon, S. : A new receptor for beta-glucans. Nature 413: 36-37, 2001.

[9758] Further studies establishing the function and utilities of CLECSF12 are found in John Hopkins OMIM database record ID 606264, and in cited publications numbered 910-913 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deoxyguanosine Kinase (DGUOK, Accession NM_080915) is another VGAM121 host target gene. DGUOK BINDING SITE1 and DGUOK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DGUOK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGUOK BINDING SITE1 and DGUOK BINDING SITE2, designated SEQ ID:28134 and SEQ ID:28138 respectively, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9759] Another function of VGAM121 is therefore inhibition of

Deoxyguanosine Kinase (DGUOK, Accession NM_080915), a gene which is deoxyguanosine kinase and mediates phosphorylation of several deoxyribonucleosides. Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGUOK. The function of DGUOK has been established by previous studies. Mitochondrial DNA depletion syndromes (OMIM Ref. No. 251880) are phenotypically heterogeneous, autosomal recessive disorders characterized by tissue-specific reduction in mtDNA copy number. Affected individuals with the hepatocerebral form of mtDNA depletion syndrome have early progressive liver failure and neurologic abnormalities, hypoglycemia, and increased lactate in body fluids. Affected tissues show both decreased activity of the mtDNA-encoded respiratory chain complexes (I, III, IV, and V) and mtDNA depletion. Mandel et al. (2001) used homozygosity mapping in 3 kindreds of Druze origin to map the hepatocerebral mtDNA depletion syndrome locus to a region of 6.1 cM on chromosome 2p13. This interval encompasses the DGUOK gene. They identified a 1-bp deletion (601465.0001) within the DGUOK gene that segregated with the disease in the 3 kindreds studied. Western blot analysis failed to

detect DGK protein in the liver of affected persons. The main supply of deoxyribonucleotides (dNTPs) for mtDNA synthesis comes from the salvage pathway initiated by DGK and thymidine kinase-2 (TK2; 188250). The association of mtDNA depletion with mutated DGUOK suggested that the salvage pathway enzymes are involved in the maintenance of balanced mitochondrial dNTP pools. In 2 German brothers with the hepatocerebral form of mitochondrial DNA-depletion syndrome (OMIM Ref. No. 251880) characterized by lactic acidosis, hepatomegaly, hypoglycemia, jaundice, and encephalopathy with hypotonia, hyperreflexia, and nystagmus, Taanman et al. (2002) identified a homozygous nonsense mutation in exon 3 of the DGUOK gene, 313C-T, resulting in a 173-amino acid truncation at the C terminus of the protein product. The unaffected parents were heterozygous for the mutation.

[9760] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9761] Mandel, H.; Szargel, R.; Labay, V.; Elpeleg, O.; Saada, A.; Shalata, A.; Anbinder, Y.; Berkowitz, D.; Hartman, C.; Barak, M.; Eriksson, S.; Cohen, N. : The deoxyguanosine kinase gene is mutated in individuals with depleted hepa-

tocerebral mitochondrial DNA. Nature Genet. 29: 337–341, 2001. Note: Erratum: Nature Genet. 29: 491 only, 2001. ; and

[9762] Taanman, J.-W.; Kateeb, I.; Muntau, A. C.; Jaksch, M.; Cohen, N.; Mandel, H. : A novel mutation in the deoxyguanosine kinase gene causing depletion of mitochondrial DNA. Ann. Neurol. 5.

[9763] Further studies establishing the function and utilities of DGUOK are found in John Hopkins OMIM database record ID 601465, and in cited publications numbered 275 and 10086 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sperm Associated Antigen 6 (SPAG6, Accession NM_012443) is another VGAM121 host target gene. SPAG6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPAG6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPAG6 BINDING SITE, designated SEQ ID:14817, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9764] Another function of VGAM121 is therefore inhibition of

Sperm Associated Antigen 6 (SPAG6, Accession NM_012443). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPAG6. Tensin (TNS, Accession NM_022648) is another VGAM121 host target gene. TNS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNS BINDING SITE, designated SEQ ID:22901, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9765] Another function of VGAM121 is therefore inhibition of Tensin (TNS, Accession NM_022648). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNS. FLJ10759 (Accession NM_018207) is another VGAM121 host target gene. FLJ10759 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10759, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ10759 BINDING SITE, designated SEQ ID:20099, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9766] Another function of VGAM121 is therefore inhibition of FLJ10759 (Accession NM_018207). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10759. FLJ10815 (Accession NM_018231) is another VGAM121 host target gene. FLJ10815 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10815, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10815 BINDING SITE, designated SEQ ID:20172, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9767] Another function of VGAM121 is therefore inhibition of FLJ10815 (Accession NM_018231). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10815. FLJ11259 (Accession NM_018370) is another VGAM121

host target gene. FLJ11259 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11259, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11259 BINDING SITE, designated SEQ ID:20381, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9768] Another function of VGAM121 is therefore inhibition of FLJ11259 (Accession NM_018370). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11259. FLJ30567 (Accession NM_145022) is another VGAM121 host target gene. FLJ30567 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30567 BINDING SITE, designated SEQ ID:29632, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9769] Another function of VGAM121 is therefore inhibition of FLJ30567 (Accession NM_145022). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30567. KIAA1361 (Accession XM_030845) is another VGAM121 host target gene. KIAA1361 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1361, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1361 BINDING SITE, designated SEQ ID:31164, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9770] Another function of VGAM121 is therefore inhibition of KIAA1361 (Accession XM_030845). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1361. LEAP-2 (Accession NM_052971) is another VGAM121 host target gene. LEAP-2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LEAP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEAP-2 BINDING SITE, designated SEQ ID:27544, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9771] Another function of VGAM121 is therefore inhibition of LEAP-2 (Accession NM_052971). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEAP-2. P1P373C6 (Accession NM_019110) is another VGAM121 host target gene. P1P373C6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P1P373C6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P1P373C6 BINDING SITE, designated SEQ ID:21187, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9772] Another function of VGAM121 is therefore inhibition of P1P373C6 (Accession NM_019110). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

P1P373C6. Protein Tyrosine Phosphatase Type IVA, Member 1 (PTP4A1, Accession NM_003463) is another VGAM121 host target gene. PTP4A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTP4A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A1 BINDING SITE, designated SEQ ID:9531, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9773] Another function of VGAM121 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 1 (PTP4A1, Accession NM_003463). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTP4A1. Unc-5 Homolog D (C. elegans) (UNC5D, Accession NM_080872) is another VGAM121 host target gene. UNC5D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC5D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of UNC5D BINDING SITE, designated SEQ ID:28113, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9774] Another function of VGAM121 is therefore inhibition of Unc-5 Homolog D (*C. elegans*) (UNC5D, Accession NM_080872). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5D. LOC143287 (Accession XM_096410) is another VGAM121 host target gene. LOC143287 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143287 BINDING SITE, designated SEQ ID:40343, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9775] Another function of VGAM121 is therefore inhibition of LOC143287 (Accession XM_096410). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC143287. LOC145678 (Accession XM_096832) is another VGAM121 host target gene. LOC145678 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145678 BINDING SITE, designated SEQ ID:40553, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9776] Another function of VGAM121 is therefore inhibition of LOC145678 (Accession XM_096832). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145678. LOC149506 (Accession XM_097661) is another VGAM121 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41003, to the nucleotide sequence of VGAM121 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2832.

[9777] Another function of VGAM121 is therefore inhibition of LOC149506 (Accession XM_097661). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149506. LOC153020 (Accession XM_087578) is another VGAM121 host target gene. LOC153020 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153020 BINDING SITE, designated SEQ ID:39352, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9778] Another function of VGAM121 is therefore inhibition of LOC153020 (Accession XM_087578). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153020. LOC255394 (Accession XM_170710) is another VGAM121 host target gene. LOC255394 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255394, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255394 BINDING SITE, designated SEQ ID:45480, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9779] Another function of VGAM121 is therefore inhibition of LOC255394 (Accession XM_170710). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255394. LOC84549 (Accession NM_032509) is another VGAM121 host target gene. LOC84549 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC84549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84549 BINDING SITE, designated SEQ ID:26257, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9780] Another function of VGAM121 is therefore inhibition of LOC84549 (Accession NM_032509). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC84549. LOC92391 (Accession XM_044793) is another VGAM121 host target gene. LOC92391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92391 BINDING SITE, designated SEQ ID:34272, to the nucleotide sequence of VGAM121 RNA, herein designated VGAM RNA, also designated SEQ ID:2832.

[9781] Another function of VGAM121 is therefore inhibition of LOC92391 (Accession XM_044793). Accordingly, utilities of VGAM121 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92391. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 122 (VGAM122) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9782] VGAM122 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM122 was detected is described hereinabove with reference to Figs. 1–8.

[9783] VGAM122 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9784] VGAM122 gene encodes a VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM122 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM122 precursor RNA is designated SEQ ID:108, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:108 is located at position 205407 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9785] VGAM122 precursor RNA folds onto itself, forming VGAM122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9786] An enzyme complex designated DICER COMPLEX, `dices` the VGAM122 folded precursor RNA into VGAM122 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM122 RNA is designated SEQ ID:2833, and is provided hereinbelow with reference to the sequence listing part.

[9787] VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM122 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[9788] VGAM122 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM122 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM122 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9789] The complementary binding of VGAM122 RNA, herein designated VGAM RNA, to host target binding sites on VGAM122 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM122 host target RNA into VGAM122 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9790] It is appreciated that VGAM122 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM122 host target genes. The mRNA of each one of this plurality of VGAM122 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM122 RNA, herein designated VGAM RNA, and which when bound by VGAM122 RNA causes inhibition of translation of respective one or more VGAM122 host target proteins.

[9791] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM122 gene, herein designated VGAM GENE, on one or more VGAM122 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9792] It is yet further appreciated that a function of VGAM122 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM122 correlate with, and may be deduced from, the identity of the host target genes which VGAM122 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [9793] Nucleotide sequences of the VGAM122 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM122 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM122 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM122 are further described hereinbelow with reference to Table 1.
- [9794] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM122 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM122 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [9795] As mentioned hereinabove with reference to Fig. 1, a function of VGAM122 gene, herein designated VGAM is inhibition of expression of VGAM122 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM122 correlate with, and may be deduced from, the identity of the target genes which VGAM122 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [9796] CREBBP/EP300 Inhibitory Protein 1 (CRI1, Accession

NM_014335) is a VGAM122 host target gene. CRI1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRI1 BINDING SITE, designated SEQ ID:15647, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9797] A function of VGAM122 is therefore inhibition of CREBBP/EP300 Inhibitory Protein 1 (CRI1, Accession NM_014335), a gene which regulates cell cycle as well as tissue-specific transcription and differentiation. Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRI1. The function of CRI1 has been established by previous studies. Miyake et al. (2000) and MacLellan et al. (2000) simultaneously reported isolating cDNAs encoding CRI1, which both groups designated EID1, using yeast 2-hybrid screens with various RB1 fragments as bait. Sequence analysis predicted that the 187-amino acid protein contains 2 acid patches and a C-terminal RB1-binding motif (LXCXE). Northern blot analysis detected ubiquitous ex-

pression of CRI1, with strongest expression in heart, skeletal muscle, and brain. Binding analysis showed that the acid patches and C terminus of CRI1 interacted with RB1 in transfected cells. Overexpression of CRI1 in a skeletal muscle cell line inhibited cell differentiation without reversing the expression of myogenic phenotype markers. Luciferase reporter analysis showed that CRI1 expression inhibits MYOD (OMIM Ref. No. 159970)-dependent transcription through multiple domains and its interaction with EP300 and CREBBP, but CRI1 expression does not affect cell cycle reentry. Miyake et al. (2000) determined that CRI1 interacts with MDM2 (OMIM Ref. No. 164785), leading to the ubiquitination and destruction of CRI1 and thereby coupling cell cycle exit to the execution of a differentiation program.

[9798] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9799] Miyake, S.; Sellers, W. R.; Safran, M.; Li, X.; Zhao, W.; Grossman, S. R.; Gan, J.; DeCaprio, J. A.; Adams, P. D.; Kaelin, W. G., Jr. : Cells degrade a novel inhibitor of differentiation with E1A-like properties upon exiting the cell cycle. *Molec. Cell. Biol.* 20: 8889-8902, 2000. ; and

[9800] MacLellan, W. R.; Xiao, G.; Abdellatif, M.; Schneider, M. D. :
A novel Rb- and p300-binding protein inhibits transactivation by MyoD. *Molec. Cell. Biol.* 20: 8903-8915, 2000.

[9801] Further studies establishing the function and utilities of CRI1 are found in John Hopkins OMIM database record ID 605894, and in cited publications numbered 4766-4768 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190) is another VGAM122 host target gene. TAPBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAPBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAPBP BINDING SITE, designated SEQ ID:9182, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9802] Another function of VGAM122 is therefore inhibition of TAP Binding Protein (tapasin) (TAPBP, Accession NM_003190), a gene which is involved in MHC class I-restricted antigen processing. Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with TAPBP. The function of TAPBP has been established by previous studies. Newly assembled major histocompatibility complex (MHC) class I molecules (see OMIM Ref. No. 142800), together with the endoplasmic reticulum (ER) chaperone calreticulin (OMIM Ref. No. 109091), interact with the transporter associated with antigen processing (TAP1; 170260) through a molecule called tapasin (Sadasivan et al., 1996). By molecular cloning of tapasin, Ortmann et al. (1997) found it to be a type I transmembrane glycoprotein encoded by an MHC-linked gene. The mature protein has 428 amino acids with a single N-linked glycosylation site at position 233. It is a member of the immunoglobulin superfamily with a probable cytoplasmic ER retention signal. Up to 4 MHC class I/tapasin complexes were found to bind to each TAP molecule in Daudi and L001 cells. Expression of tapasin in a negative mutant human cell line restored class I/TAP association and normal class I cell surface expression. Tapasin expression also corrected the defective recognition of virus-infected cells of the same line by class I-restricted cytotoxic T cells, thus establishing a critical functional role for tapasin in MHC class I-restricted antigen processing. Herberg et al. (1998) iden-

tified an EST encoding the mouse tapasin homolog. Mayer and Klein (2001) proposed that tapasin is in reality an MHC class I molecule with a different function from that currently executed by conventional class I molecules. They based this proposal on the amino acid sequence similarity between tapasin and conventional class I molecules, on similarity of predicted tertiary structure and domain organization of the molecules, on similarity of exon/intron organization of the encoding genes, and on the mapping of the class IA and tapasin genes into the same chromosomal region in all jawed vertebrates that had been tested to that time (Michalova et al., 2000).

[9803] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9804] Mayer, W. E.; Klein, J. : Is tapasin a modified Mhc class I molecule? Immunogenetics 53: 719–723, 2001. ; and

[9805] Ortmann, B.; Copeman, J.; Lehner, P. J.; Sadasivan, B.; Herberg, J. A.; Grandea, A. G.; Riddell, S. R.; Tampe, R.; Spies, T.; Trowsdale, J.; Cresswell, P. : A critical role for tapasin.

[9806] Further studies establishing the function and utilities of TAPBP are found in John Hopkins OMIM database record ID 601962, and in cited publications numbered

5822–5828 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 5 (double-strand-break rejoining; Ku autoantigen, 80kDa) (XRCC5, Accession NM_021141) is another VGAM122 host target gene. XRCC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC5 BINDING SITE, designated SEQ ID:22114, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9807] Another function of VGAM122 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 5 (double-strand-break rejoining; Ku autoantigen, 80kDa) (XRCC5, Accession NM_021141), a gene which is one subunit of the Ku protein complex, which binds to DNA ends and regulates DNA-dependent protein kinase. Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC5. The function of XRCC5 has

been established by previous studies. The human XRCC5 DNA repair gene complements the radiosensitive mutant xrs-6, derived from Chinese hamster ovary cells which are defective in DNA double-strand break repair and in ability to undergo V(D)J recombination. The XRCC5 gene encodes the 80-kD subunit of the Ku autoantigen, a heterodimer which contributes to genomic integrity through its ability to bind DNA double-strand breaks and facilitate repair by the nonhomologous end-joining pathway. Tuteja et al. (1994) purified from HeLa cells an enzyme they called DNA helicase II, an ATP-dependent DNA unwinding enzyme. They showed that it is a heterodimer of 72 and 87 kD polypeptides. Sequencing showed that it is identical to the Ku autoantigen. The exclusively nuclear location of this particular DNA helicase II/Ku antigen, its highly specific affinity for double-stranded DNA, its abundance, and its exclusive DNA-duplex unwinding activity pointed to additional roles for this molecule in DNA metabolism. Animal model experiments lend further support to the function of XRCC5. Difilippantonio et al. (2000) demonstrated that mouse cells deficient for Ku80 display a marked increase in chromosomal aberrations, including breakage, translocations, and aneuploidy. Despite the observed

chromosome instabilities, Ku80 $-/-$ mice have only a slightly earlier onset of cancer. Loss of p53 (OMIM Ref. No. 191170) synergizes with Ku80 to promote tumorigenesis such that all Ku80 $-/-$ /p53 $-/-$ mice succumb to disseminated pro-B-cell lymphoma before 3 months of age. Tumors result from a specific set of chromosomal translocations and gene amplifications involving IgH and c-Myc, reminiscent of Burkitt lymphoma (OMIM Ref. No. 113970). Difilippantonio et al. (2000) concluded that Ku80 is a caretaker gene that maintains the integrity of the genome by a mechanism involving suppression of chromosomal rearrangements.

[9808] It is appreciated that the abovementioned animal model for XRCC5 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9809] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9810] Difilippantonio, M. J.; Zhu, J.; Chen, H. T.; Meffre, E.; Nussenzweig, M. C.; Max, E. E.; Ried, T.; Nussenzweig, A. : DNA repair protein Ku80 suppresses chromosomal aberrations and malignant transformation. Nature 404:

510–514, 2000. ; and

[9811] Tuteja, N.; Tuteja, R.; Ochem, A.; Taneja, P.; Huang, N. W.; Simoncsits, A.; Susic, S.; Rahman, K.; Marusic, L.; Chen, J.; Zhang, J.; Wang, S.; Pongor, S.; Falaschi, A. : Human DNA heli.

[9812] Further studies establishing the function and utilities of XRCC5 are found in John Hopkins OMIM database record ID 194364, and in cited publications numbered 6048, 6051, 6054–6056, 183 and 6057–1840 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. HDAC9–PENDING (Accession NM_014707) is another VGAM122 host target gene. HDAC9–PENDING BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HDAC9–PENDING, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC9–PENDING BINDING SITE, designated SEQ ID:16250, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9813] Another function of VGAM122 is therefore inhibition of HDAC9–PENDING (Accession NM_014707). Accordingly,

utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC9-PENDING. KIAA0121 (Accession XM_052386) is another VGAM122 host target gene. KIAA0121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0121 BINDING SITE, designated SEQ ID:35967, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9814] Another function of VGAM122 is therefore inhibition of KIAA0121 (Accession XM_052386). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0121. KIAA0620 (Accession XM_030707) is another VGAM122 host target gene. KIAA0620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0620 BINDING SITE, designated SEQ ID:31123, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9815] Another function of VGAM122 is therefore inhibition of KIAA0620 (Accession XM_030707). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0620. KIAA1550 (Accession XM_039393) is another VGAM122 host target gene. KIAA1550 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1550, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1550 BINDING SITE, designated SEQ ID:33073, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9816] Another function of VGAM122 is therefore inhibition of KIAA1550 (Accession XM_039393). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1550. PRO0461 (Accession NM_031268) is another VGAM122 host target gene. PRO0461 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO0461, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0461 BINDING SITE, designated SEQ ID:25285, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9817] Another function of VGAM122 is therefore inhibition of PRO0461 (Accession NM_031268). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0461. LOC118738 (Accession XM_061125) is another VGAM122 host target gene. LOC118738 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC118738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118738 BINDING SITE, designated SEQ ID:37193, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9818] Another function of VGAM122 is therefore inhibition of

LOC118738 (Accession XM_061125). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118738. LOC203536 (Accession XM_114716) is another VGAM122 host target gene. LOC203536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203536 BINDING SITE, designated SEQ ID:43055, to the nucleotide sequence of VGAM122 RNA, herein designated VGAM RNA, also designated SEQ ID:2833.

[9819] Another function of VGAM122 is therefore inhibition of LOC203536 (Accession XM_114716). Accordingly, utilities of VGAM122 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203536. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 123 (VGAM123) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[9820] VGAM123 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM123 was detected is described hereinabove with reference to Figs. 1–8.

[9821] VGAM123 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9822] VGAM123 gene encodes a VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM123 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM123 precursor RNA is designated SEQ ID:109, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:109 is located at position 246206 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9823] VGAM123 precursor RNA folds onto itself, forming VGAM123 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[9824] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM123 folded precursor RNA into VGAM123 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 43%) nucleotide se-
quence of VGAM123 RNA is designated SEQ ID:2834, and
is provided hereinbelow with reference to the sequence
listing part.

[9825] VGAM123 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM123 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM123 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9826] VGAM123 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM123 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM123 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9827] The complementary binding of VGAM123 RNA, herein designated VGAM RNA, to host target binding sites on VGAM123 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM123 host target RNA into VGAM123 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9828] It is appreciated that VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM123 host target genes. The mRNA of each one of this plurality of VGAM123 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM123 RNA, herein designated VGAM RNA, and which when bound by VGAM123 RNA causes inhibition of translation of respective one or more VGAM123 host target proteins.

[9829] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM123 gene, herein designated VGAM GENE, on one or more VGAM123 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9830] It is yet further appreciated that a function of VGAM123 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM123 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM123 correlate with, and may be deduced from, the identity of the host target genes which VGAM123 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[9831] Nucleotide sequences of the VGAM123 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM123 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM123 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM123 are further described hereinbelow with reference to Table 1.

[9832] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM123 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM123 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9833] As mentioned hereinabove with reference to Fig. 1, a function of VGAM123 gene, herein designated VGAM is inhibition of expression of VGAM123 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM123 correlate with, and may be deduced from, the identity of the target genes which VGAM123 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[9834] Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 1 (NFATC1, Accession NM_006162) is a VGAM123 host target gene. NFATC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFATC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFATC1 BINDING SITE, designated SEQ ID:12813, to the nucleotide sequence of VGAM123 RNA, herein designated VGAM RNA, also designated SEQ ID:2834.

[9835] A function of VGAM123 is therefore inhibition of Nuclear Factor of Activated T-cells, Cytoplasmic, Calcineurin-dependent 1 (NFATC1, Accession NM_006162), a gene which regulates the activation, proliferation, differentiation and programmed death of lymphoid and nonlymphoid cells. Accordingly, utilities of VGAM123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFATC1. The function of NFATC1 has been established by previous studies. Jauliac et al. (2002) found that both NFATC1 and NFAT5 (OMIM Ref. No. 604708) were expressed in invasive human ductal breast

carcinomas. Using cell lines derived from breast and colon carcinomas, they found that these NFATs promoted carcinoma invasion and that their activity correlated with expression of alpha-6 (OMIM Ref. No. 147556)/beta-4 (OMIM Ref. No. 147557) integrin. Animal model experiments lend further support to the function of NFATC1. Whereas *Nfatc1*-deficient mice have impaired proliferative and Th2-like responses, *Nfatc2*-deficient mice have modestly enhanced responses with Th2-like characteristics. By fetal liver chimerization in *Rag2* (OMIM Ref. No. 179616)-deficient hosts, Peng et al. (2001) generated mice whose lymphocytes were deficient in both transcription factors. Functional analysis showed that the double knockout (DKO) mice had reasonable proliferative responses and expression of activation markers but were incapable of producing a wide range of cytokines, with the exception of weak production of IL5 (OMIM Ref. No. 147850), and of expressing CD40 ligand (CD40LG; 300386) and CD95 ligand (CD95L; 134638) or allogeneic cytotoxicity. Analysis of serum immunoglobulins revealed significantly elevated amounts of IgG1 and IgE, isotypes typically associated with Th2-like immune responses, in DKO mice. The results suggested that NFATC1 and

NFATC2 are essential for the maintenance of B-cell homeostasis and differentiation, but are dispensable for T-cell inflammatory activity, as measured by lymphoproliferation and activation marker expression

[9836] It is appreciated that the abovementioned animal model for NFATC1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9837] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9838] Peng, S. L.; Gerth, A. J.; Ranger, A. M.; Glimcher, L. H. : NFATc1 and NFATc2 together control both T and B cell activation and differentiation. *Immunity* 14: 13–20, 2001.
; and

[9839] Jauliac, S.; Lopez-Rodriguez, C.; Shaw, L. M.; Brown, L. F.; Rao, A.; Toker, A. : The role of NFAT transcription factors in integrin-mediated carcinoma invasion. *Nature Cell Biol.* 4: 540–5.

[9840] Further studies establishing the function and utilities of NFATC1 are found in John Hopkins OMIM database record ID 600489, and in cited publications numbered 9903–9908, 11673–991 and 11674 listed in the bibliog–

raphy section hereinbelow, which are also hereby incorporated by reference. Nidogen (enactin) (NID, Accession NM_002508) is another VGAM123 host target gene. NID BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NID, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NID BINDING SITE, designated SEQ ID:8338, to the nucleotide sequence of VGAM123 RNA, herein designated VGAM RNA, also designated SEQ ID:2834.

[9841] Another function of VGAM123 is therefore inhibition of Nidogen (enactin) (NID, Accession NM_002508). Accordingly, utilities of VGAM123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NID. Solute Carrier Family 19, Member 3 (SLC19A3, Accession NM_025243) is another VGAM123 host target gene. SLC19A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC19A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC19A3 BINDING SITE,

designated SEQ ID:24924, to the nucleotide sequence of VGAM123 RNA, herein designated VGAM RNA, also designated SEQ ID:2834.

[9842] Another function of VGAM123 is therefore inhibition of Solute Carrier Family 19, Member 3 (SLC19A3, Accession NM_025243). Accordingly, utilities of VGAM123 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC19A3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 124 (VGAM124) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9843] VGAM124 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM124 was detected is described hereinabove with reference to Figs. 1–8.

[9844] VGAM124 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9845] VGAM124 gene encodes a VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM124 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM124 precursor RNA is designated SEQ ID:110, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:110 is located at position 232082 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9846] VGAM124 precursor RNA folds onto itself, forming VGAM124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9847] An enzyme complex designated DICER COMPLEX, `dices` the VGAM124 folded precursor RNA into VGAM124 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM124 RNA is designated SEQ ID:2835, and is provided hereinbelow with reference to the sequence listing part.

[9848] VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM124 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9849] VGAM124 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM124 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM124 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9850] The complementary binding of VGAM124 RNA, herein designated VGAM RNA, to host target binding sites on VGAM124 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM124 host target RNA into VGAM124 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9851] It is appreciated that VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM124 host target genes. The mRNA of each one of this plurality of VGAM124 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM124 RNA, herein designated VGAM RNA, and which when bound by VGAM124 RNA causes inhibition of translation of respective one or more VGAM124 host target proteins.

[9852] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM124 gene, herein designated VGAM GENE, on one or more VGAM124 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9853] It is yet further appreciated that a function of VGAM124 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM124 correlate with, and may be deduced from, the identity of the host target genes which VGAM124 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9854] Nucleotide sequences of the VGAM124 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM124 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM124 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM124 are further described hereinbelow with reference to Table 1.

[9855] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM124 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM124 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9856] As mentioned hereinabove with reference to Fig. 1, a function of VGAM124 gene, herein designated VGAM is inhibition of expression of VGAM124 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM124 correlate with, and may be deduced from, the identity of the target genes which VGAM124 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9857] Glucosamine-6-phosphate Isomerase (GNPI, Accession NM_005471) is a VGAM124 host target gene. GNPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNPI BINDING SITE, designated SEQ ID:11965, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM

RNA, also designated SEQ ID:2835.

[9858] A function of VGAM124 is therefore inhibition of Glucosamine-6-phosphate Isomerase (GNPI, Accession NM_005471), a gene which converts glucosamine-6-phosphate to fructose-6-phosphate. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNPI. The function of GNPI has been established by previous studies. In the course of investigating hexosamine catabolism in the human malaria parasite, *Plasmodium falciparum*, Weidanz et al. (1995) became aware of deficiencies in understanding the relevant enzymatic reactions in the host erythrocyte. For that reason, they undertook studies of human glucosamine 6-phosphate deaminase using a newly developed sensitive radiometric assay. They characterized biochemically the erythrocyte enzyme and reported data on its kinetics, temperature stability, and chromatographic purification. Weidanz et al. (1995) noted that the nucleotide sequence of the nagB gene, encoding the deaminase in *E. coli* K12, has been determined (Rogers et al. (1988)) but information about the primary structure of the mammalian enzyme was not available. The hamster sperm oscillin protein is responsible for

oocyte calcium oscillations. By screening a testis cDNA library for a homolog of hamster oscillin, Shevchenko et al. (1998) obtained a cDNA encoding GNPI. The deduced 289-amino acid protein is 96% identical to the hamster sequence. SDS-PAGE and Western blot analysis indicated that GNPI is expressed as a 33-kD cytosolic protein in various cell lines. Functional analysis showed that GNPI has glucosamine 6-phosphate deaminase activity but does not induce calcium oscillations in mammalian eggs. Genomic sequence analysis determined that the single-copy GNPI gene contains 8 exons.

[9859] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9860] Shevchenko, V.; Hogben, M.; Ekong, R.; Parrington, J.; Lai, F. A. : The human glucosamine-6-phosphate deaminase gene: cDNA cloning and expression, genomic organization and chromosomal localization. *Gene* 216: 31-38, 1998. ; and

[9861] Weidanz, J. A.; Campbell, P.; DeLucas, L. J.; Jin, J.; Moore, D.; Roden, L.; Yu, H.; Heilmann, E.; Vezza, A. C. : Glucosamine 6-phosphate deaminase in normal human erythrocytes. *Brit. J.*

[9862] Further studies establishing the function and utilities of GNPI are found in John Hopkins OMIM database record ID 601798, and in cited publications numbered 6244–6247 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. G Protein–coupled Receptor 65 (GPR65, Accession XM_007392) is another VGAM124 host target gene. GPR65 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GPR65, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR65 BINDING SITE, designated SEQ ID:30050, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9863] Another function of VGAM124 is therefore inhibition of G Protein–coupled Receptor 65 (GPR65, Accession XM_007392). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR65. Mannose–binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242) is another VGAM124 host target gene. MBL2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by MBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBL2 BINDING SITE, designated SEQ ID:5761, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9864] Another function of VGAM124 is therefore inhibition of Mannose-binding Lectin (protein C) 2, Soluble (opsonic defect) (MBL2, Accession NM_000242). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBL2. Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM_002655) is another VGAM124 host target gene. PLAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLAG1 BINDING SITE, designated SEQ ID:8521, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9865] Another function of VGAM124 is therefore inhibition of

Pleiomorphic Adenoma Gene 1 (PLAG1, Accession NM_002655), a gene which contains a zinc finger domain. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLAG1. The function of PLAG1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM29. Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM_006922) is another VGAM124 host target gene. SCN3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN3A BINDING SITE, designated SEQ ID:13796, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9866] Another function of VGAM124 is therefore inhibition of Sodium Channel, Voltage-gated, Type III, Alpha Polypeptide (SCN3A, Accession NM_006922), a gene which may be important for maintaining neural membrane excitabil-

ity. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN3A. The function of SCN3A has been established by previous studies. On physical mapping by pulsed field gel electrophoresis in the mouse, Malo et al. (1991) demonstrated that the Scn2a (OMIM Ref. No. 182390) and Scn3a genes encoding type II and type III sodium channel alpha-subunit isoforms, respectively, are physically linked and are separated by a maximum distance of 600 kb. The gene for type II maps to chromosome 2 in both mouse and man; hence, SCN3A in the human must be located on chromosome 2. Ahmed et al. (1992) isolated 2 cDNAs from a human cerebral cortex library by screening for the presence of sodium channel alpha-subunit-specific clones. One of the clones showed greatest homology to rat brain sodium channel II. The second clone encoded a different subtype sodium channel, probably a type III channel. Both of the genes were mapped to human chromosome 2 by study of human-hamster somatic cell hybrids; PCR with primers derived from the second cDNA was used for localizing the gene, which presumably was SCN3A. By in situ hybridization, both of the genes mapped to 2q23-q24.3. Malo et al.

(1994) mapped the SCN3A gene to chromosome 2 with 100% concordance using PCR on human/rodent somatic cell hybrid panels. By fluorescence in situ hybridization, they mapped the gene to 2q24–q31.

[9867] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9868] Malo, D.; Schurr, E.; Dorfman, J.; Canfield, V.; Levenson, R.; Gros, P. : Three brain sodium channel alpha–subunit genes are clustered on the proximal segment of mouse chromosome 2. Genomics 10: 666–672, 1991. ; and

[9869] Malo, M. S.; Srivastava, K.; Andresen, J. M.; Chen, X.–N.; Korenberg, J. R.; Ingram, V. M. : Targeted gene walking by low stringency polymerase chain reaction: assignment of a putative.

[9870] Further studies establishing the function and utilities of SCN3A are found in John Hopkins OMIM database record ID 182391, and in cited publications numbered 75 and 885–886 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TEM7 (Accession NM_020405) is another VGAM124 host target gene. TEM7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

TEM7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM7 BINDING SITE, designated SEQ ID:21672, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9871] Another function of VGAM124 is therefore inhibition of TEM7 (Accession NM_020405), a gene which involves in angiogenesis. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM7. The function of TEM7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM23.Tryptase, Alpha (TPS1, Accession XM_018104) is another VGAM124 host target gene. TPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TPS1 BINDING SITE, designated SEQ ID:30336, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA,

also designated SEQ ID:2835.

[9872] Another function of VGAM124 is therefore inhibition of Tryptase, Alpha (TPS1, Accession XM_018104), a gene which Alpha tryptase; mast cell-specific serine protease. Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TPS1. The function of TPS1 has been established by previous studies. Tryptase is a serine protease that is selectively concentrated in the secretory granules of mast cells and is secreted during the coupled activation-degranulation response of these cells. Its exclusive presence in mast cells permits its use as a specific clinical indicator of mast cell activation by measurement of its level in biologic fluids and as a selective marker of intact mast cells using immunohistochemical techniques with antitryptase antibodies. The enzyme is a tetramer with 4 subunits of 31,000–33,000 Da. Miller et al. (1989) cloned and sequenced human tryptase cDNA. Based on nucleic acid sequence, human tryptase consists of a 244-amino acid catalytic portion of 27,423 Da with 2 putative N-linked carbohydrate-binding sites and a 30-amino acid leader sequence of 3,048 Da. Vanderslice et al. (1990) demonstrated the existence of multiple

trypsinases. In this respect, mast cell trypsinase is like other serine proteases such as glandular kallikrein (OMIM Ref. No. 147960) and trypsin (OMIM Ref. No. 276000), which are also members of multigene families. Miller et al. (1990) mapped both alpha-trypsinase and beta-trypsinase (OMIM Ref. No. 191081) to human chromosome 16 by PCR analysis of DNA from human/hamster somatic cell hybrids.

[9873] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9874] Miller, J. S.; Westin, E. H.; Schwartz, L. B. : Cloning and characterization of complementary DNA for human trypsinase. J. Clin. Invest. 84: 1188–1195, 1989. ; and

[9875] Vanderslice, P.; Ballinger, S. M.; Tam, E. K.; Goldstein, S. M.; Craik, C. S.; Caughey, G. H. : Human mast cell trypsinase: multiple cDNAs and genes reveal a multigene serine protease fami.

[9876] Further studies establishing the function and utilities of TPS1 are found in John Hopkins OMIM database record ID 191080, and in cited publications numbered 9772–9774 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.CSR1 (Accession

NM_016240) is another VGAM124 host target gene. CSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSR1 BINDING SITE, designated SEQ ID:18355, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9877] Another function of VGAM124 is therefore inhibition of CSR1 (Accession NM_016240). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSR1. DKFZP564F013 (Accession XM_168479) is another VGAM124 host target gene. DKFZP564F013 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564F013, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564F013 BINDING SITE, designated SEQ ID:45202, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9878] Another function of VGAM124 is therefore inhibition of DKFZP564F013 (Accession XM_168479). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564F013. FLJ13072 (Accession XM_117117) is another VGAM124 host target gene. FLJ13072 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13072 BINDING SITE, designated SEQ ID:43235, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9879] Another function of VGAM124 is therefore inhibition of FLJ13072 (Accession XM_117117). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13072. KIAA1238 (Accession XM_048675) is another VGAM124 host target gene. KIAA1238 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1238 BINDING SITE, designated SEQ ID:35213, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9880] Another function of VGAM124 is therefore inhibition of KIAA1238 (Accession XM_048675). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1238. NYD-SP11 (Accession NM_031951) is another VGAM124 host target gene. NYD-SP11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NYD-SP11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP11 BINDING SITE, designated SEQ ID:25690, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9881] Another function of VGAM124 is therefore inhibition of NYD-SP11 (Accession NM_031951). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-

SP11. RP4-622L5 (Accession NM_019118) is another VGAM124 host target gene. RP4-622L5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RP4-622L5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RP4-622L5 BINDING SITE, designated SEQ ID:21199, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9882] Another function of VGAM124 is therefore inhibition of RP4-622L5 (Accession NM_019118). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RP4-622L5. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617) is another VGAM124 host target gene. SLC11A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A2 BINDING SITE, designated SEQ

ID:6221, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9883] Another function of VGAM124 is therefore inhibition of Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A2. UQCR (Accession NM_006830) is another VGAM124 host target gene. UQCR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UQCR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UQCR BINDING SITE, designated SEQ ID:13709, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9884] Another function of VGAM124 is therefore inhibition of UQCR (Accession NM_006830). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UQCR. LOC146958 (Accession XM_097142) is another VGAM124

host target gene. LOC146958 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146958 BINDING SITE, designated SEQ ID:40772, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9885] Another function of VGAM124 is therefore inhibition of LOC146958 (Accession XM_097142). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146958. LOC147004 (Accession XM_097155) is another VGAM124 host target gene. LOC147004 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147004, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147004 BINDING SITE, designated SEQ ID:40780, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9886] Another function of VGAM124 is therefore inhibition of LOC147004 (Accession XM_097155). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147004. LOC153592 (Accession XM_098396) is another VGAM124 host target gene. LOC153592 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153592, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153592 BINDING SITE, designated SEQ ID:41648, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9887] Another function of VGAM124 is therefore inhibition of LOC153592 (Accession XM_098396). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153592. LOC220776 (Accession XM_043388) is another VGAM124 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33929, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9888] Another function of VGAM124 is therefore inhibition of LOC220776 (Accession XM_043388). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC220827 (Accession XM_166052) is another VGAM124 host target gene. LOC220827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220827 BINDING SITE, designated SEQ ID:43845, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9889] Another function of VGAM124 is therefore inhibition of LOC220827 (Accession XM_166052). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC220827. LOC221814 (Accession XM_168226) is another VGAM124 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45096, to the nucleotide sequence of VGAM124 RNA, herein designated VGAM RNA, also designated SEQ ID:2835.

[9890] Another function of VGAM124 is therefore inhibition of LOC221814 (Accession XM_168226). Accordingly, utilities of VGAM124 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 125 (VGAM125) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9891] VGAM125 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM125 was detected is described hereinabove with reference to Figs. 1–8.

[9892] VGAM125 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9893] VGAM125 gene encodes a VGAM125 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM125 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM125 precursor RNA is designated SEQ ID:111, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:111 is located at position 36670 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9894] VGAM125 precursor RNA folds onto itself, forming VGAM125 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9895] An enzyme complex designated DICER COMPLEX, `dices` the VGAM125 folded precursor RNA into VGAM125 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM125 RNA is designated SEQ ID:2836, and is provided hereinbelow with reference to the sequence listing part.

[9896] VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM125 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9897] VGAM125 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM125 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM125 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[9898] The complementary binding of VGAM125 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM125 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM125 host target RNA into VGAM125 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9899] It is appreciated that VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM125 host target genes. The mRNA of each one of this plurality of VGAM125 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM125 RNA, herein designated VGAM RNA, and which when bound by VGAM125 RNA causes inhibition of translation of respective one or more VGAM125 host target proteins.

[9900] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM125 gene, herein designated VGAM GENE, on one or more VGAM125 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9901] It is yet further appreciated that a function of VGAM125 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM125 correlate with, and may be deduced from, the identity of the host target genes which VGAM125 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9902] Nucleotide sequences of the VGAM125 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM125 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM125 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM125 are further
described hereinbelow with reference to Table 1.

[9903] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM125 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM125 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[9904] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM125 gene, herein designated VGAM is
inhibition of expression of VGAM125 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM125 correlate with, and may be deduced
from, the identity of the target genes which VGAM125
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[9905] Endometrial Bleeding Associated Factor (left-right deter-
mination, factor A; transforming growth factor beta su-

perfamily) (EBAF, Accession XM_037302) is a VGAM125 host target gene. EBAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EBAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EBAF BINDING SITE, designated SEQ ID:32608, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9906] A function of VGAM125 is therefore inhibition of Endometrial Bleeding Associated Factor (left-right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM_037302), a gene which LEFT-RIGHT AXIS MALFORMATIONS. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EBAF. The function of EBAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM93. Glypican 1 (GPC1, Accession NM_002081) is another VGAM125 host target gene. GPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by GPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC1 BINDING SITE, designated SEQ ID:7874, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9907] Another function of VGAM125 is therefore inhibition of Glypican 1 (GPC1, Accession NM_002081), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC1. The function of GPC1 has been established by previous studies. Cell surface heparan sulfate proteoglycans are composed of a membrane-associated protein core substituted with a variable number of heparan sulfate chains. Two different cell surface heparan sulfate proteoglycan families can be distinguished: (1) the syndecan-like integral membrane proteoglycans (SLIPS), with a core protein spanning the cytoplasmic membrane, and (2) the glypican-related integral membrane proteoglycans (GRIPS), with a core protein anchored to the cytoplasmic membrane via a glycosyl phosphatidylinositol.

Vermeesch et al. (1995) mapped the gene encoding glypican, the only human glypiated heparan sulfate proteoglycan that had so far been identified by cloning. By fluorescence in situ hybridization, they assigned the gene to 2q35–q37. Endostatin (OMIM Ref. No. 120328), a collagen XVIII fragment, is a potent antiangiogenic protein. Karumanchi et al. (2001) showed that alkaline phosphatase-tagged endostatin bound endothelial cells, revealing 2 binding affinities. Expression cloning identified glypican, specifically glypican–1 or glypican–4 (OMIM Ref. No. 300168), as the lower-affinity receptor. Biochemical and genetic studies indicated that the heparan sulfate glycosaminoglycans of glypican were critical for endostatin binding. Furthermore, endostatin selected a specific octasulfated hexasaccharide from a sequence in heparin. Karumanchi et al. (2001) also demonstrated a role for endostatin in renal tubular cell branching morphogenesis and showed that glypicans serve as low-affinity receptors for endostatin in these cells, as in endothelial cells. Anti-sense experiments suggested the critical importance of glypicans in mediating endostatin activities.

[9908] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [9909] Karumanchi, S. A.; Jha, V.; Ramchandran, R.; Karihaloo, A.; Tsiokas, L.; Chan, B.; Dhanabal, M.; Hanai, J.; Venkataraman, G.; Shriver, Z.; Keiser, N.; Kalluri, R.; and 9 others : Cell surface glypicans are low-affinity endostatin receptors. *Molec. Cell* 7: 811–822, 2001. ; and
- [9910] Vermeesch, J. R.; Mertens, G.; David, G.; Marynen, P. : Assignment of the human glypican gene (GPC1) to 2q35–q37 by fluorescence in situ hybridization. *Genomics* 25: 327–329, 1995.
- [9911] Further studies establishing the function and utilities of GPC1 are found in John Hopkins OMIM database record ID 600395, and in cited publications numbered 7251 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2A (GRIN2A, Accession NM_000833) is another VGAM125 host target gene. GRIN2A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRIN2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRIN2A BINDING SITE, designated SEQ

ID:6488, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9912] Another function of VGAM125 is therefore inhibition of Glutamate Receptor, Ionotropic, N-methyl D-aspartate 2A (GRIN2A, Accession NM_000833), a gene which modulates the efficiency of synaptic plasticity. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRIN2A. The function of GRIN2A has been established by previous studies. Molecular cloning and expression of cDNAs demonstrate that the epsilon and zeta subfamilies of the mouse glutamate receptor channel subunits constitute NMDA (N-methyl-D-aspartate) receptor channels (see OMIM Ref. No. GRIN2D; 602717). Four members of the epsilon subfamily, the E1, E2 (GRIN2B; 138252), E3 (GRIN2C; 138254), and E4 (OMIM Ref. No. GRIN2D) subunits, are distinct in distribution, functional properties, and regulation. Thus, the molecular diversity of the epsilon subunit family probably underlies the functional heterogeneity of the NMDA receptor channel. Rat counterparts of the mouse E1, E2, E3, E4, and zeta-1 (Z1; GRIN1, 138249) subunits were also isolated and designated as

Nr2a, Nr2b, Nr2c, Nr2d, and Nmdar1, respectively (Monyer et al., 1992; Ishii et al., 1993). Animal model experiments lend further support to the function of GRIN2A. Sakimura et al. (1995) showed that targeted disruption of the mouse Nmdar2a gene produced mice that were viable, although impaired hippocampal plasticity was observed in homozygous $-/-$ mice. By gene targeting, Sprengel et al. (1998) generated mutant mice expressing the Nmdar2a gene without the large intracellular C-terminal domain. These mice were viable but exhibited impaired synaptic plasticity and contextual memory. The authors concluded that the observed phenotypes appear to reflect defective intracellular signaling.

[9913] It is appreciated that the abovementioned animal model for GRIN2A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9914] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9915] Monyer, H.; Sprengel, R.; Schoepfer, R.; Herb, A.; Higuchi, M.; Lomeli, H.; Burnashev, N.; Sakmann, B.; Seeburg, P. H. : Heteromeric NMDA receptors: molecular and functional

distinction of subtypes. Science 256: 1217–1221, 1992. ;
and

[9916] Sakimura, K.; Kutsuwada, T.; Ito, I.; Manabe, T.; Takayama, C.; Kushiya, E.; Yagi, T.; Aizawa, S.; Inoue, Y.; Sugiyama, H.; Mishina, M. : Reduced hippocampal LTP and spatial learning in.

[9917] Further studies establishing the function and utilities of GRIN2A are found in John Hopkins OMIM database record ID 138253, and in cited publications numbered 3598, 1457–1460, 145 and 3599 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Heterogeneous Nuclear Ribonucleoprotein K (HNRPK, Accession NM_002140) is another VGAM125 host target gene. HNRPK BINDING SITE1 and HNRPK BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by HNRPK, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPK BINDING SITE1 and HNRPK BINDING SITE2, designated SEQ ID:7915 and SEQ ID:25279 respectively, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9918] Another function of VGAM125 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein K (HNRPK, Accession NM_002140), a gene which play a role in the nuclear metabolism of hnRNAs, particularly for pre-mRNAs that contain cytidine-rich sequence. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPK. The function of HNRPK has been established by previous studies. The hnRNP-K family of acidic nuclear proteins have been identified using a monoclonal antibody that distinguishes between quiescent and proliferating human keratinocytes. The family, which is composed of at least 4 major proteins (e.g.: 164017, 600124, 164020, and HNRPD) and their modified forms, is present in similar overall levels in quiescent and proliferating normal keratinocytes, although clear differences were observed in levels of some of the individual variants. Using a monoclonal antibody as a probe, Dejgaard et al. (1994) cloned a cDNA coding for type B hnRNP-K, and this was used to screen for additional family members. Sequencing of positive clones revealed 4 alternative splicing variants of a gene that mapped to chromosome 9 (by Southern blot analysis of human/rodent somatic cell hybrids). The hnRNP-K protein

has been implicated in pre-mRNA metabolism of transcripts containing cytidine-rich sequences, and the results of Dejgaard et al. (1994) point toward a role in cell cycle progression. Tommerup and Leffers (1996) mapped HNRNPK to 9q21.32-q21.33 by fluorescence in situ hybridization.

- [9919] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9920] Dejgaard, K.; Leffers, H.; Rasmussen, H. H.; Madsen, P.; Kruse, T. A.; Gesser, B.; Nielsen, H.; Celis, J. E. : Identification, molecular cloning, expression and chromosome mapping of a family of transformation upregulated hnRNP-K proteins derived by alternative splicing. J. Molec. Biol. 236: 33-48, 1994. ; and
- [9921] Tommerup, N.; Leffers, H. : Assignment of human KH-box-containing genes by in situ hybridization: HNRNPK maps to 9q21.32-q21.33, PCBP1 to 2p12-p13, and PCBP2 to 12q13.12-q13.13, distal to F.
- [9922] Further studies establishing the function and utilities of HNRNPK are found in John Hopkins OMIM database record ID 600712, and in cited publications numbered 10049-10050 listed in the bibliography section hereinbe-

low, which are also hereby incorporated by reference. MAX Binding Protein (MNT, Accession NM_020310) is another VGAM125 host target gene. MNT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MNT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MNT BINDING SITE, designated SEQ ID:21564, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9923] Another function of VGAM125 is therefore inhibition of MAX Binding Protein (MNT, Accession NM_020310). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MNT. Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350) is another VGAM125 host target gene. PDGFRB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRB

BINDING SITE, designated SEQ ID:32815, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9924] Another function of VGAM125 is therefore inhibition of Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350), a gene which Platelet-derived growth factor receptor beta chain; tyrosine kinase receptor. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRB. The function of PDGFRB has been established by previous studies. Steer and Cross (2002) reviewed the acquired reciprocal chromosomal translocations that involve 5q31-q33 and are associated with a significant minority of patients with BCR-ABL-negative chronic myeloid leukemias. The most common of these fuses the ETV6 gene to the PDGFRB gene, but at the time of the review 4 additional partner genes were known: H4 (D10S170), HIP1, CEV14 (OMIM Ref. No. TRIP11), and rabaptin-5. Clinically, most patients present with a myeloproliferative disorder with eosinophilia, eosinophilic leukemia, or chronic myelomonocytic leukemia and thus fall into the broad category of myeloproliferative disorders/myelodysplastic

syndromes (MPD/MDS). With the advent of targeted signal transduction therapy, patients with rearrangement of PDGFRB might be better classified as a distinct subgroup of MPD/MDS. Animal model experiments lend further support to the function of PDGFRB. Klinghoffer et al. (2001) created 2 complementary lines of knockin mice in which the intracellular signaling domains of one PDGFR had been removed and replaced by those of the other PDGFR. While both lines demonstrated substantial rescue of normal development, substitution of the *Pdgfrb* signaling domains with those of *Pdgfra* resulted in varying degrees of vascular disease.

[9925] It is appreciated that the abovementioned animal model for PDGFRB is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[9926] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9927] Klinghoffer, R. A.; Mueting-Nelsen, P. F.; Faerman, A.; Shani, M.; Soriano, P. : The two PDGF receptors maintain conserved signaling in vivo despite divergent embryological functions. *Molec. Cell* 7: 343–354, 2001. ; and

- [9928] Steer, E. J.; Cross, N. C. P. : Myeloproliferative disorders with translocations of chromosome 5q31–35: role of the platelet–derived growth factor receptor beta. *Acta Haemat.* 107: 113–.
- [9929] Further studies establishing the function and utilities of PDGFRB are found in John Hopkins OMIM database record ID 173410, and in cited publications numbered 3526, 4606–3529, 11281, 5108–3535, 3822–353 and 3826 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphatidylinositol Glycan, Class K (PIGK, Accession XM_039644) is another VGAM125 host target gene. PIGK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIGK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGK BINDING SITE, designated SEQ ID:33135, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.
- [9930] Another function of VGAM125 is therefore inhibition of Phosphatidylinositol Glycan, Class K (PIGK, Accession XM_039644), a gene which catalyzes the transfer of fully

assembled GPI units to proteins. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGK. The function of PIGK has been established by previous studies. Glycosylphosphatidylinositol (GPI) anchors are synthesized in the endoplasmic reticulum and posttranslationally added to N-terminally processed proteins, replacing C-terminal sequences at a specific upstream omega site. This final step consists of a transamidation reaction. By searching an EST database for sequences similar to yeast Gpi8, Benghezal et al. (1996) identified a cDNA encoding PIGK, which they called GPI8. Sequence analysis predicted that the 396-amino acid PIGK protein shares 43% amino acid identity with yeast Gpi8. Yu et al. (1997) identified a mutant cell line that fails to incorporate GPI anchors into nascent N-terminally processed proproteins due to a defect in transamidation. By PCR analysis using the PIGK sequence reported by Benghezal et al. (1996), Yu et al. (1997) identified additional upstream sequences, including an ATG initiation codon. Expression of this PIGK cDNA in the mutant cell line restored GPI anchor assembly. Northern blot analysis detected major 1.6- and 1.9-kb PIGK transcripts in HeLa and K562 cell lines. Southern blot

analysis of genomic DNA indicated that PIGK is a single gene spanning 20 to 25 kb. By somatic cell hybrid analysis, Yu et al. (1997) mapped the PIGK gene to chromosome 1.

[9931] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9932] Benghezal, M.; Benachour, A.; Rusconi, S.; Aebi, M.; Conzelmann, A. : Yeast Gpi8p is essential for GPI anchor attachment onto proteins. EMBO J. 15: 6575–6583, 1996. ; and

[9933] Yu, J.; Nagarajan, S.; Knez, J. J.; Udenfriend, S.; Chen, R.; Medof, M. E. : The affected gene underlying the class K glycosylphosphatidylinositol (GPI) surface protein defect codes for.

[9934] Further studies establishing the function and utilities of PIGK are found in John Hopkins OMIM database record ID 605087, and in cited publications numbered 6605–6606 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prostaglandin F2 Receptor Negative Regulator (PTGFRN, Accession XM_040709) is another VGAM125 host target gene. PT-GFRN BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by PTGFRN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGFRN BINDING SITE, designated SEQ ID:33365, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9935] Another function of VGAM125 is therefore inhibition of Prostaglandin F₂ Receptor Negative Regulator (PTGFRN, Accession XM_040709), a gene which inhibits the binding of prostaglandin f₂-alpha (pgf₂- alpha) to its specific fp receptor. Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGFRN. The function of PTGFRN has been established by previous studies. Orlicky et al. (1996) isolated a protein that copurifies with bovine prostaglandin F-2-alpha receptor (FP) and cloned the corresponding rat cDNA. Transfection experiments suggested that this protein inhibits binding of PGF-2-alpha to FP. Histologically, this protein (called FP regulatory protein, or FPRP, by them) shows a distribution coinciding well with those cells and tissues that respond to PGF-2-alpha.

- [9936] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9937] Nagase, T.; Kikuno, R.; Ishikawa, K.; Hirosawa, M.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XVI. The complete sequences of 150 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 7: 65–73, 2000. ; and
- [9938] Stipp et al. (2001) used moderately stringent Brij96/97 detergent extraction to show that FPRP associates specifically with CD81 and CD9 but not with other tetraspanin molecules, such as C.
- [9939] Further studies establishing the function and utilities of PTGFRN are found in John Hopkins OMIM database record ID 601204, and in cited publications numbered 6370–6373 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TR2 (Accession XM_051264) is another VGAM125 host target gene. TR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se–

quences of TR2 BINDING SITE, designated SEQ ID:35795, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9940] Another function of VGAM125 is therefore inhibition of TR2 (Accession XM_051264), a gene which maintains high levels of reduced glutathione in the cytosol (by similarity). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TR2. The function of TR2 has been established by previous studies. Members of the tumor necrosis factor receptor (TNFR) family play a key role in regulating the immune response to infection (see OMIM Ref. No. TNFR1, 191190). By screening for genes that mediate the entry of herpes simplex virus (HSV) into Chinese hamster ovary (CHO) cells, Montgomery et al. (1996) identified cDNAs encoding a member of the TNFR family. They designated the gene HVEM (herpesvirus entry mediator). The predicted 283-amino acid protein had characteristics of a type I membrane glycoprotein, with an N-terminal signal peptide, 2 potential sites for addition of N-linked glycans, and a putative membrane-spanning domain. Sequence analysis revealed that HVEM contained a cysteine-rich repeat region characteristic of TNFR family members, and

shared 17 to 25% amino acid identity with other TNFRs. Montgomery et al. (1996) suggested that HVEM plays an important role in HSV pathogenesis because it enhanced the entry of several wildtype HSV strains of both serotypes into CHO cells, and mediated HSV entry into activated human T cells. Independently, Kwon et al. (1997) cloned cDNAs encoding HVEM, which they designated TR2. Northern blot analysis revealed that HVEM is expressed as a 1.7-kb mRNA in several tissues, with the highest expression in lung, spleen, and thymus. Several additional larger mRNAs were observed in some tissues and several of the cDNAs contained insertions in the coding region, leading Kwon et al. (1997) to suggest that HVEM is regulated at the level of mRNA maturation. These authors reported that the in vitro translation product was 32 kD by SDS-PAGE. Marsters et al. (1997) also identified HVEM as a novel member of the TNFR family. The authors attributed differences between their predicted amino acid sequence and that of Montgomery et al. (1996) to polymorphism. Using epitope-tagged HVEM, Marsters et al. (1997) found that HVEM interacted in vivo with several TNFR-associated factor (TRAF) proteins, including TRAF1 (OMIM Ref. No. 601711), TRAF2 (OMIM Ref. No. 601895), TRAF3 (OMIM Ref. No.

601896), and TRAF5 (OMIM Ref. No. 602356). Expression of HVEM activated JNK1 (OMIM Ref. No. 601158), NF- κ -B (see OMIM Ref. No. 164011), and AP1 (OMIM Ref. No. 165160), which control expression of multiple genes in response to infection or cellular stress. Marsters et al. (1997) concluded that HVEM is linked via TRAFs to signal transduction pathways that activate the immune response. Hsu et al. (1997) cloned cDNAs for the mouse HVEM homolog, which they designated ATAR (another TRAF-associated receptor). The predicted 276-amino acid mouse protein shares only 45% protein sequence identity with human HVEM. By flow cytometric and RT-PCR analysis, Morel et al. (2000) showed that the expression of the HVEM ligand, LIGHT (TNFSF14; 604520), is upregulated, whereas HVEM expression is downregulated, after T-cell activation, particularly CD8-positive T-cell activation. HSV infection requires binding of the viral envelope glycoprotein D (gD) to cell surface receptors. Carfi et al. (2001) reported the x-ray structures of a soluble, truncated ectodomain of gD both alone and in complex with the ectodomain of its cellular receptor, TNFRSF14, which they called HVEA. Two bound anions suggested possible binding sites for another gD receptor, a 3-O-sulfonated hep-

aran sulfate. The structures revealed a V-like immunoglobulin fold at the core of gD that is closely related to cellular adhesion molecules and flanked by large N- and C-terminal extensions. The receptor-binding segment of gD, an N-terminal hairpin, appeared conformationally flexible, suggesting that a conformational change accompanying binding might be part of the viral entry mechanism. By fluorescence in situ hybridization, Kwon et al. (1997) mapped the HVEM gene to 1p36.3–p36.2. This region also contains the TNFR genes CD30 (OMIM Ref. No. 153243), ILA (OMIM Ref. No. 602250), TXGP1L (OMIM Ref. No. 600315), and TNFR2 (OMIM Ref. No. 191191), suggesting that HVEM evolved through a localized gene duplication event.

[9941] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9942] Carfi, A.; Willis, S. H.; Whitbeck, J. C.; Krummenacher, C.; Cohen, G. H.; Eisenberg, R. J.; Wiley, D. C. : Herpes simplex virus glycoprotein D bound to the human receptor HveA. *Molec. Cell* 8: 169–179, 2001. ; and

[9943] Morel, Y.; Schiano de Colella, J.-M.; Harrop, J.; Deen, K. C.; Holmes, S. D.; Wattam, T. A.; Khandekar, S. S.; Truneh, A.;

Sweet, R. W.; Gastaut, J.-A.; Olive, D.; Costello, R. T. : Rec.

[9944] Further studies establishing the function and utilities of TR2 are found in John Hopkins OMIM database record ID 602746, and in cited publications numbered 2402–2403, 2406–240 and 2407 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BCL2–associated Athanogene 5 (BAG5, Accession NM_004873) is another VGAM125 host target gene. BAG5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BAG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG5 BINDING SITE, designated SEQ ID:11307, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9945] Another function of VGAM125 is therefore inhibition of BCL2–associated Athanogene 5 (BAG5, Accession NM_004873). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG5. BM–002 (Accession NM_016617) is another VGAM125 host target gene. BM–002 BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by BM-002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BM-002 BINDING SITE, designated SEQ ID:18724, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9946] Another function of VGAM125 is therefore inhibition of BM-002 (Accession NM_016617). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BM-002. Chromosome 8 Open Reading Frame 4 (C8orf4, Accession NM_020130) is another VGAM125 host target gene. C8orf4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf4 BINDING SITE, designated SEQ ID:21325, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9947] Another function of VGAM125 is therefore inhibition of Chromosome 8 Open Reading Frame 4 (C8orf4, Accession NM_020130). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf4. CDW92 (Accession NM_080546) is another VGAM125 host target gene. CDW92 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDW92, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDW92 BINDING SITE, designated SEQ ID:27866, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9948] Another function of VGAM125 is therefore inhibition of CDW92 (Accession NM_080546). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDW92. DKFZP564I1171 (Accession XM_049568) is another VGAM125 host target gene. DKFZP564I1171 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564I1171, correspond-

ing to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I1171 BINDING SITE, designated SEQ ID:35445, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9949] Another function of VGAM125 is therefore inhibition of DKFZP564I1171 (Accession XM_049568). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I1171. DKFZp761J1523 (Accession NM_032293) is another VGAM125 host target gene. DKFZp761J1523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761J1523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761J1523 BINDING SITE, designated SEQ ID:26061, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9950] Another function of VGAM125 is therefore inhibition of DKFZp761J1523 (Accession NM_032293). Accordingly,

utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761J1523. FLJ11155 (Accession NM_018342) is another VGAM125 host target gene. FLJ11155 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11155 BINDING SITE, designated SEQ ID:20347, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9951] Another function of VGAM125 is therefore inhibition of FLJ11155 (Accession NM_018342). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11155. KIAA1237 (Accession XM_087386) is another VGAM125 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE,

designated SEQ ID:39220, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9952] Another function of VGAM125 is therefore inhibition of KIAA1237 (Accession XM_087386). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. KIAA1376 (Accession XM_033042) is another VGAM125 host target gene. KIAA1376 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1376, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1376 BINDING SITE, designated SEQ ID:31821, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9953] Another function of VGAM125 is therefore inhibition of KIAA1376 (Accession XM_033042). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1376. KIAA1416 (Accession XM_098762) is another VGAM125 host target gene. KIAA1416 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1416 BINDING SITE, designated SEQ ID:41810, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9954] Another function of VGAM125 is therefore inhibition of KIAA1416 (Accession XM_098762). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1416. KIAA1913 (Accession XM_058167) is another VGAM125 host target gene. KIAA1913 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1913, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1913 BINDING SITE, designated SEQ ID:36576, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9955] Another function of VGAM125 is therefore inhibition of

KIAA1913 (Accession XM_058167). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1913. MGC19556 (Accession NM_033551) is another VGAM125 host target gene. MGC19556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC19556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC19556 BINDING SITE, designated SEQ ID:27317, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9956] Another function of VGAM125 is therefore inhibition of MGC19556 (Accession NM_033551). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC19556. MGC8407 (Accession NM_024046) is another VGAM125 host target gene. MGC8407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC8407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC8407 BINDING SITE, designated SEQ ID:23479, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9957] Another function of VGAM125 is therefore inhibition of MGC8407 (Accession NM_024046). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC8407. MORF4 (Accession XM_165470) is another VGAM125 host target gene. MORF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MORF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MORF4 BINDING SITE, designated SEQ ID:43643, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9958] Another function of VGAM125 is therefore inhibition of MORF4 (Accession XM_165470). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MORF4. Protein Phosphatase 1A (formerly 2C), Magnesium-depen-

dent, Alpha Isoform (PPM1A, Accession NM_021003) is another VGAM125 host target gene. PPM1A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPM1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPM1A BINDING SITE, designated SEQ ID:21997, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9959] Another function of VGAM125 is therefore inhibition of Protein Phosphatase 1A (formerly 2C), Magnesium-dependent, Alpha Isoform (PPM1A, Accession NM_021003). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPM1A. PRO1430 (Accession NM_018599) is another VGAM125 host target gene. PRO1430 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRO1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1430 BINDING SITE, designated SEQ ID:20675, to the

nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9960] Another function of VGAM125 is therefore inhibition of PRO1430 (Accession NM_018599). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1430. LOC119369 (Accession XM_061434) is another VGAM125 host target gene. LOC119369 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC119369, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC119369 BINDING SITE, designated SEQ ID:37207, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9961] Another function of VGAM125 is therefore inhibition of LOC119369 (Accession XM_061434). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC119369. LOC126302 (Accession XM_059020) is another VGAM125 host target gene. LOC126302 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC126302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126302 BINDING SITE, designated SEQ ID:36824, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9962] Another function of VGAM125 is therefore inhibition of LOC126302 (Accession XM_059020). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126302. LOC129676 (Accession XM_065341) is another VGAM125 host target gene. LOC129676 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129676, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129676 BINDING SITE, designated SEQ ID:37284, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9963] Another function of VGAM125 is therefore inhibition of LOC129676 (Accession XM_065341). Accordingly, utilities

of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129676. LOC144667 (Accession XM_096648) is another VGAM125 host target gene. LOC144667 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144667 BINDING SITE, designated SEQ ID:40450, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9964] Another function of VGAM125 is therefore inhibition of LOC144667 (Accession XM_096648). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144667. LOC146756 (Accession XM_097085) is another VGAM125 host target gene. LOC146756 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC146756 BINDING SITE, designated SEQ ID:40739, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9965] Another function of VGAM125 is therefore inhibition of LOC146756 (Accession XM_097085). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146756. LOC152275 (Accession XM_098186) is another VGAM125 host target gene. LOC152275 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152275, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152275 BINDING SITE, designated SEQ ID:41458, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9966] Another function of VGAM125 is therefore inhibition of LOC152275 (Accession XM_098186). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152275. LOC162083 (Accession XM_091339) is another VGAM125 host target gene. LOC162083 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162083, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162083 BINDING SITE, designated SEQ ID:40047, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9967] Another function of VGAM125 is therefore inhibition of LOC162083 (Accession XM_091339). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162083. LOC200982 (Accession XM_117305) is another VGAM125 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43375, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9968] Another function of VGAM125 is therefore inhibition of

LOC200982 (Accession XM_117305). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. LOC245728 (Accession XM_165922) is another VGAM125 host target gene. LOC245728 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245728, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245728 BINDING SITE, designated SEQ ID:43800, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9969] Another function of VGAM125 is therefore inhibition of LOC245728 (Accession XM_165922). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245728. LOC254015 (Accession XM_172977) is another VGAM125 host target gene. LOC254015 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC254015 BINDING SITE, designated SEQ ID:46246, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9970] Another function of VGAM125 is therefore inhibition of LOC254015 (Accession XM_172977). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254015. LOC257106 (Accession XM_170910) is another VGAM125 host target gene. LOC257106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257106 BINDING SITE, designated SEQ ID:45678, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9971] Another function of VGAM125 is therefore inhibition of LOC257106 (Accession XM_170910). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257106. LOC57109 (Accession NM_020385) is an-

other VGAM125 host target gene. LOC57109 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57109 BINDING SITE, designated SEQ ID:21656, to the nucleotide sequence of VGAM125 RNA, herein designated VGAM RNA, also designated SEQ ID:2836.

[9972] Another function of VGAM125 is therefore inhibition of LOC57109 (Accession NM_020385). Accordingly, utilities of VGAM125 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57109. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 126 (VGAM126) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[9973] VGAM126 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM126 was detected is described

hereinabove with reference to Figs. 1–8.

[9974] VGAM126 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[9975] VGAM126 gene encodes a VGAM126 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM126 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM126 precursor RNA is designated SEQ ID:112, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:112 is located at position 47516 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[9976] VGAM126 precursor RNA folds onto itself, forming VGAM126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[9977] An enzyme complex designated DICER COMPLEX, `dices` the VGAM126 folded precursor RNA into VGAM126 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM126 RNA is designated SEQ ID:2837, and is provided hereinbelow with reference to the sequence listing part.

[9978] VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM126 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[9979] VGAM126 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM126 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM126 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[9980] The complementary binding of VGAM126 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM126 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM126 host target RNA into VGAM126 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[9981] It is appreciated that VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM126 host target genes. The mRNA of each one of this plurality of VGAM126 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM126 RNA, herein designated VGAM RNA, and which when bound by VGAM126 RNA causes inhibition of translation of respective one or more VGAM126 host target proteins.

[9982] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM126 gene, herein designated VGAM GENE, on one or more VGAM126 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[9983] It is yet further appreciated that a function of VGAM126 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM126 correlate with, and may be deduced from, the identity of the host target genes which VGAM126 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[9984] Nucleotide sequences of the VGAM126 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM126 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM126 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM126 are further described hereinbelow with reference to Table 1.

[9985] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM126 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM126 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[9986] As mentioned hereinabove with reference to Fig. 1, a function of VGAM126 gene, herein designated VGAM is inhibition of expression of VGAM126 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM126 correlate with, and may be deduced from, the identity of the target genes which VGAM126 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[9987] UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_006057) is a VGAM126 host target gene. B3GALT5 BINDING SITE1

through B3GALT5 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by B3GALT5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GALT5 BINDING SITE1 through B3GALT5 BINDING SITE5, designated SEQ ID:12701, SEQ ID:27029, SEQ ID:27034, SEQ ID:27039 and SEQ ID:27024 respectively, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[9988] A function of VGAM126 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,3-galactosyltransferase, Polypeptide 5 (B3GALT5, Accession NM_006057). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GALT5. GATA Binding Protein 2 (GATA2, Accession NM_002050) is another VGAM126 host target gene. GATA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of GATA2 BINDING SITE, designated SEQ ID:7800, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[9989] Another function of VGAM126 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM_002050). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM_003949) is another VGAM126 host target gene. HAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HAP1 BINDING SITE, designated SEQ ID:10072, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[9990] Another function of VGAM126 is therefore inhibition of Huntingtin-associated Protein 1 (neuroan 1) (HAP1, Accession NM_003949), a gene which functions as an adaptor protein using coiled coils to mediate interactions

among cytoskeletal, vascular, and motor proteins. Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HAP1. The function of HAP1 has been established by previous studies. Several neurodegenerative disorders are known to involve trinucleotide expansions of the CAG codon for glutamine, including Huntington disease (HD; 143100), spinocerebellar ataxia type 1 (OMIM Ref. No. 164400), Machado–Joseph disease (OMIM Ref. No. 109150), and spinobulbar muscular atrophy (313700.0014). Li et al. (1995) identified a cDNA for a rat brain protein that binds to the mutant HD protein by using the latter as bait in a 2–hybrid yeast screening assay. The protein, which they designated HAP1 (huntingtin–associated protein–1), was found to bind to huntingtin in proportion to the number of glutamines present in the glutamine repeat region. Two HAP1 cDNAs were found that differ at the C terminus, probably as a result of alternative splicing. The predicted 599– and 629–amino acid proteins are highly hydrophilic, rich in charged amino acids, and have no homology to known proteins. Two human PCR products, termed HAP1 and HLP (HAP–like protein), were obtained. The human HAP1 cDNA

encoded a protein 96% identical to the rat HAP1 protein. Northern blots showed a 4.0-kb HAP1 transcript in rat brains and RT-PCR demonstrated expression in human brain, especially in the caudate and cortex, regions affected in Huntington disease. Coimmunoprecipitation experiments with rat brain tissue and HAP1-transfected cells confirmed that HAP1 binds to huntingtin in vivo, though they had not yet clearly shown the same in human brain tissue. Li et al. (1995) speculated that the ability of HAP1 to bind to glutamine repeats in huntingtin is influenced by adjacent amino acids, since in their yeast 2-hybrid assays there was no binding of HAP1 to atrophin-1, even though their atrophin-1 construct contained essentially the same number of glutamine repeats (21) as did their huntingtin construct (23). Animal model experiments lend further support to the function of HAP1. Bertaux et al. (1998) cloned mouse Hap1 cDNA and demonstrated that expression is not enriched in areas specifically affected in Huntington disease. Bertaux et al. (1998) used the yeast 2-hybrid system to demonstrate that amino acids 171-230 of the huntingtin-associated protein are necessary for hap1-huntingtin binding and that Hap1 does not interact with the transgene exon 1 protein in a transgenic

model of HD.

- [9991] It is appreciated that the abovementioned animal model for HAP1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.
- [9992] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [9993] Li, X.-J.; Li, S.-H.; Sharp, A. H.; Nucifora, F. C., Jr.; Schilling, G.; Lanahan, A.; Worley, P.; Snyder, S. H.; Ross, C. A. : A huntingtin-associated protein enriched in brain with implications for pathology. *Nature* 378: 398–402, 1995. ; and
- [9994] Bertaux, F.; Sharp, A. H.; Ross, C. A.; Lehrach, H.; Bates, G. P.; Wanker, E. : HAP1–huntingtin interactions do not contribute to the molecular pathology in Huntington's disease transgen.
- [9995] Further studies establishing the function and utilities of HAP1 are found in John Hopkins OMIM database record ID 600947, and in cited publications numbered 9614–9619 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 7

(KCNA7, Accession NM_031886) is another VGAM126 host target gene. KCNA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNA7 BINDING SITE, designated SEQ ID:25626, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[9996] Another function of VGAM126 is therefore inhibition of Potassium Voltage-gated Channel, Shaker-related Subfamily, Member 7 (KCNA7, Accession NM_031886), a gene which allows nerve cells to efficiently repolarize following an action potential. Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNA7. The function of KCNA7 has been established by previous studies. See 176260 for a general discussion of potassium voltage-gated ion channels. Using a probe from the mouse in the study of somatic cell hybrids, McPherson et al. (1991) found that a seventh member of the Shaker-related potassium voltage-gated channel is encoded by a gene on

chromosome 19. Kalman et al. (1998) reported the isolation of the mouse voltage-gated Shaker-related potassium channel gene, Kv1.7 (Kcna7). Unlike other known Kv1 family genes that have intronless coding regions, the protein-coding region of Kv1.7 was interrupted by a 1.9-kb intron. The gene was mapped to mouse chromosome 7 and human chromosome 19q13.3. The mouse Kv1.7 channel was voltage-dependent and exhibited cumulative inactivation. Northern blot analysis revealed transcripts of approximately 3 kb in mouse heart and skeletal muscle. Bardien-Kruger et al. (2002) deduced the coding region of KCNA7 by aligning the mouse cDNA sequence with a human BAC clone and mouse EST sequences. The region encodes a protein of 456 amino acid residues containing cytoplasmic N- and C-termini, a central core domain composed of 6 transmembrane segments and the characteristic pore-loop. The human intron was 1153 bp in length and smaller than that of mouse (1929 bp). Using the deduced amino acid sequences, the potassium-channels of the 2 species were highly conserved (greater than 95%). The expression of KCNA7 in human adult heart was confirmed by RT-PCR studies. Bardien-Kruger et al. (2002) refined the location of the KCNA7

gene within chromosome 19q13.3 by bioinformatic in silico mapping and implicated it as a positional candidate gene for progressive familial heart block type I (OMIM Ref. No. 604559), an autosomal dominant cardiac conduction disorder mapped to 19q13.3. In affected individuals, Bardien-Kruger et al. (2002) screened the coding region of KCNA7 by PCR-SSCP analysis and direct DNA sequencing, which did not reveal any pathogenic sequence changes

[9997] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[9998] Bardien-Kruger, S.; Wulff, H.; Arieff, Z.; Brink, P.; Chandy, K. G.; Corfield, V. : Characterisation of the human voltage-gated potassium channel gene, KCNA7, a candidate gene for inherited cardiac disorders, and its exclusion as cause of progressive familial heart block I (PFHBI). *Europ. J. Hum. Genet.* 10: 36-43, 2002. ; and

[9999] Kalman, K.; Nguyen, A.; Tseng-Crank, J.; Dukes, I. D.; Chandy, G.; Hustad, C. M.; Copeland, N. G.; Jenkins, N. A.; Mohrenweiser, H.; Brandriff, B.; Cahalan, M.; Gutman, G. A.; Chandy, K.

[10000] Further studies establishing the function and utilities of KCNA7 are found in John Hopkins OMIM database record

ID 176268, and in cited publications numbered 1094 and 10928 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myosin ID (MYO1D, Accession XM_050041) is another VGAM126 host target gene. MYO1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1D BINDING SITE, designated SEQ ID:35547, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10001] Another function of VGAM126 is therefore inhibition of Myosin ID (MYO1D, Accession XM_050041), a gene which is an unconventional myosin. Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO1D. The function of MYO1D has been established by previous studies. Myosins are molecular motors that, upon interaction with actin filaments, utilize energy from ATP hydrolysis to generate mechanical force. For further background information on myosins, see MYO1A (OMIM Ref. No.

601478). By screening for cDNAs with the potential to encode large proteins expressed in brain, Nagase et al. (1998) identified a cDNA encoding MYO1D, which they called KIAA0727. The deduced 674-amino acid protein is 98% identical to rat Myr4. RT-PCR analysis detected expression of KIAA0727 in all tissues tested, with highest levels in brain, followed by lung and ovary; expression was lowest in spleen.

[10002] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10003] Hasson, T.; Skowron, J. F.; Gilbert, D. J.; Avraham, K. B.; Perry, W. L.; Bement, W. M.; Anderson, B. L.; Sherr, E. H.; Chen, Z.-Y.; Greene, L. A.; Ward, D. C.; Corey, D. P.; Mooseker, M. S.; Copeland, N. G.; Jenkins, N. A. : Mapping of unconventional myosins in mouse and human. *Genomics* 36: 431-439, 1996. ; and

[10004] Nagase, T.; Ishikawa, K.; Suyama, M.; Kikuno, R.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. XI. The c.

[10005] Further studies establishing the function and utilities of MYO1D are found in John Hopkins OMIM database record

ID 606539, and in cited publications numbered 702 and 7048 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.ERG-1 (Accession NM_022034) is another VGAM126 host target gene. ERG-1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ERG-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERG-1 BINDING SITE, designated SEQ ID:22555, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10006] Another function of VGAM126 is therefore inhibition of ERG-1 (Accession NM_022034). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERG-1. FLJ10748 (Accession NM_018203) is another VGAM126 host target gene. FLJ10748 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ10748 BINDING SITE, designated SEQ ID:20084, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10007] Another function of VGAM126 is therefore inhibition of FLJ10748 (Accession NM_018203). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10748. KIAA0319 (Accession NM_014809) is another VGAM126 host target gene. KIAA0319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0319 BINDING SITE, designated SEQ ID:16757, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10008] Another function of VGAM126 is therefore inhibition of KIAA0319 (Accession NM_014809). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0319. MGC2306 (Accession NM_032638) is another

VGAM126 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26349, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10009] Another function of VGAM126 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. MGC2705 (Accession NM_032701) is another VGAM126 host target gene. MGC2705 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2705, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2705 BINDING SITE, designated SEQ ID:26416, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10010] Another function of VGAM126 is therefore inhibition of MGC2705 (Accession NM_032701). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2705. X123 (Accession XM_046023) is another VGAM126 host target gene. X123 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by X123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of X123 BINDING SITE, designated SEQ ID:34650, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10011] Another function of VGAM126 is therefore inhibition of X123 (Accession XM_046023). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with X123. LOC144453 (Accession XM_084869) is another VGAM126 host target gene. LOC144453 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC144453, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144453 BINDING SITE, designated SEQ ID:37744, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10012] Another function of VGAM126 is therefore inhibition of LOC144453 (Accession XM_084869). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144453. LOC149670 (Accession XM_086647) is another VGAM126 host target gene. LOC149670 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149670, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149670 BINDING SITE, designated SEQ ID:38804, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10013] Another function of VGAM126 is therefore inhibition of LOC149670 (Accession XM_086647). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC149670. LOC157247 (Accession XM_088275) is another VGAM126 host target gene. LOC157247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157247, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157247 BINDING SITE, designated SEQ ID:39575, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10014] Another function of VGAM126 is therefore inhibition of LOC157247 (Accession XM_088275). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157247. LOC203197 (Accession XM_114645) is another VGAM126 host target gene. LOC203197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203197 BINDING SITE, designated SEQ ID:43007, to the nucleotide sequence of VGAM126 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2837.

[10015] Another function of VGAM126 is therefore inhibition of LOC203197 (Accession XM_114645). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203197. LOC254559 (Accession XM_172931) is another VGAM126 host target gene. LOC254559 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254559 BINDING SITE, designated SEQ ID:46198, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10016] Another function of VGAM126 is therefore inhibition of LOC254559 (Accession XM_172931). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254559. LOC92661 (Accession XM_046465) is another VGAM126 host target gene. LOC92661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92661, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92661 BINDING SITE, designated SEQ ID:34721, to the nucleotide sequence of VGAM126 RNA, herein designated VGAM RNA, also designated SEQ ID:2837.

[10017] Another function of VGAM126 is therefore inhibition of LOC92661 (Accession XM_046465). Accordingly, utilities of VGAM126 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92661. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 127 (VGAM127) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10018] VGAM127 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM127 was detected is described hereinabove with reference to Figs. 1–8.

[10019] VGAM127 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syn–

drome Virus (white spot bacilliform virus). VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10020] VGAM127 gene encodes a VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM127 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM127 precursor RNA is designated SEQ ID:113, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:113 is located at position 126505 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10021] VGAM127 precursor RNA folds onto itself, forming VGAM127 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10022] An enzyme complex designated DICER COMPLEX, `dices` the VGAM127 folded precursor RNA into VGAM127 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM127 RNA is designated SEQ ID:2838, and is provided hereinbelow with reference to the sequence listing part.

[10023] VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM127 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10024] VGAM127 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM127 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM127 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10025] The complementary binding of VGAM127 RNA, herein designated VGAM RNA, to host target binding sites on VGAM127 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM127 host tar-

get RNA into VGAM127 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10026] It is appreciated that VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM127 host target genes. The mRNA of each one of this plurality of VGAM127 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM127 RNA, herein designated VGAM RNA, and which when bound by VGAM127 RNA causes inhibition of translation of respective one or more VGAM127 host target proteins.

[10027] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM127 gene, herein designated VGAM GENE, on one or more VGAM127 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10028] It is yet further appreciated that a function of VGAM127 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM127 correlate with, and may be deduced from, the identity of the host target genes which VGAM127 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10029] Nucleotide sequences of the VGAM127 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM127 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM127 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM127 are further described hereinbelow with reference to Table 1.

[10030] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM127 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM127 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10031] As mentioned hereinabove with reference to Fig. 1, a function of VGAM127 gene, herein designated VGAM is inhibition of expression of VGAM127 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM127 correlate with, and may be deduced from, the identity of the target genes which VGAM127 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10032] Multiple Endocrine Neoplasia I (MEN1, Accession NM_130803) is a VGAM127 host target gene. MEN1 BINDING SITE1 and MEN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MEN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE1 and MEN1 BINDING SITE2, designated SEQ ID:28299 and SEQ ID:28303 respectively, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10033] A function of VGAM127 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession NM_130803). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. SMP1 (Accession NM_014313) is another VGAM127 host target gene. SMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMP1 BINDING SITE, designated SEQ ID:15611, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10034] Another function of VGAM127 is therefore inhibition of SMP1 (Accession NM_014313), a gene which is a potential integral membrane protein. Accordingly, utilities of

VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMP1. The function of SMP1 has been established by previous studies. Wagner and Flegel (2000) found that the RH cluster on chromosome 1p contains 3 genes: RHD (OMIM Ref. No. 111680), RHCE (OMIM Ref. No. 111700), and SMP1. They noted that the nucleotide sequence of SMP1 had been deposited in GenBank (AF091282) as encoding a putative 157-amino acid member of an 18-kD small membrane protein family and that the gene shows homology to an open reading frame on chromosome 21 (Reboul et al., 1999). The position of the gene between both RH genes implies that any polymorphism of the SMP1 gene would be tightly linked to a specific RH haplotype. The authors suggested that functionally relevant mutations of the SMP1 gene may cause selection pressure for or against specific RH haplotypes. Such factors might explain some previously unresolved issues of RH haplotype distribution, such as the high frequency of RH-negativity in the European population.

[10035] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [10036] Reboul, J.; Gardiner, K.; Monneron, D.; Uze, G.; Lutfalla, G. : Comparative genomic analysis of the interferon/interleukin-10 receptor gene cluster. *Genome Res.* 9: 242-250, 1999. ; and
- [10037] Wagner, F. F.; Flegel, W. A. : RHD gene deletion occurred in the Rhesus box. *Blood* 95: 3662-3668, 2000.
- [10038] Further studies establishing the function and utilities of SMP1 are found in John Hopkins OMIM database record ID 605348, and in cited publications numbered 6179 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Xylulokinase Homolog (*H. influenzae*) (XYLB, Accession NM_005108) is another VGAM127 host target gene. XYLB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XYLB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XYLB BINDING SITE, designated SEQ ID:11583, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.
- [10039] Another function of VGAM127 is therefore inhibition of Xylulokinase Homolog (*H. influenzae*) (XYLB, Accession

NM_005108), a gene which is similar to *Haemophilus influenzae* xylulokinase and may play a role in energy metabolism. Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XYLB. The function of XYLB has been established by previous studies. The 3p22–p21.3 chromosomal region is one of 3 regions of 3p that is commonly deleted in various carcinomas. By analysis of a cloned segment from this region, Tamari et al. (1998) identified a novel gene, which they designated XYLB because the predicted 528–amino acid protein shares 22% identity with *Haemophilus influenzae* xylulokinase (Xyl). The XYLB gene contains 18 exons and spans approximately 28 kb. Northern blot analysis revealed that XYLB was expressed as a 2.3–kb major transcript in all tissues tested. A less abundant 1.8–kb mRNA was detected in heart and skeletal muscle. Daigo et al. (1999) reported that the XYLB gene is located between the OCTL2 (OMIM Ref. No. 604048) and ActRIIB (OMIM Ref. No. 602730) genes on 3p22–p21.3.

[10040] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [10041] Daigo, Y.; Isomura, M.; Nishiwaki, T.; Tamari, M.; Ishikawa, S.; Kai, M.; Murata, Y.; Takeuchi, K.; Yamane, Y.; Hayashi, R.; Minami, M.; Fujino, M. A.; Hojo, Y.; Uchiyama, I.; Takagi, T.; Nakamura, Y. : Characterization of a 1200-kb genomic segment of chromosome 3p22–p21.3. DNA Res. 6: 37–44, 1999. ; and
- [10042] Tamari, M.; Daigo, Y.; Ishikawa, S.; Nakamura, Y. : Genomic structure of a novel human gene (XYLB) on chromosome 3p22–p21.3 encoding a xylulokinase–like protein. Cytogenet. Cell Genet.
- [10043] Further studies establishing the function and utilities of XYLB are found in John Hopkins OMIM database record ID 604049, and in cited publications numbered 9037 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Heterogeneous Nuclear Ribonucleoprotein C (C1/C2) (HNRPC, Accession NM_031314) is another VGAM127 host target gene. HNRPC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPC BINDING SITE, designated SEQ

ID:25350, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10044] Another function of VGAM127 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein C (C1/C2) (HNRPC, Accession NM_031314). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPC. KIAA1364 (Accession XM_032997) is another VGAM127 host target gene. KIAA1364 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1364, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1364 BINDING SITE, designated SEQ ID:31815, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10045] Another function of VGAM127 is therefore inhibition of KIAA1364 (Accession XM_032997). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1364. KR18 (Accession NM_033288) is another

VGAM127 host target gene. KR18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KR18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KR18 BINDING SITE, designated SEQ ID:27122, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10046] Another function of VGAM127 is therefore inhibition of KR18 (Accession NM_033288). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KR18. LOC221103 (Accession XM_167758) is another VGAM127 host target gene. LOC221103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221103 BINDING SITE, designated SEQ ID:44777, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10047] Another function of VGAM127 is therefore inhibition of LOC221103 (Accession XM_167758). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221103. LOC90333 (Accession XM_030958) is another VGAM127 host target gene. LOC90333 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90333 BINDING SITE, designated SEQ ID:31228, to the nucleotide sequence of VGAM127 RNA, herein designated VGAM RNA, also designated SEQ ID:2838.

[10048] Another function of VGAM127 is therefore inhibition of LOC90333 (Accession XM_030958). Accordingly, utilities of VGAM127 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90333. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 128 (VGAM128) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[10049] VGAM128 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM128 was detected is described hereinabove with reference to Figs. 1–8.

[10050] VGAM128 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10051] VGAM128 gene encodes a VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM128 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM128 precursor RNA is designated SEQ ID:114, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:114 is located at position 46000 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10052] VGAM128 precursor RNA folds onto itself, forming

VGAM128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10053] An enzyme complex designated DICER COMPLEX, `dices` the VGAM128 folded precursor RNA into VGAM128 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM128 RNA is designated SEQ ID:2839, and is provided hereinbelow with reference to the sequence listing part.

[10054] VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM128 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10055] VGAM128 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM128 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM128 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10056] The complementary binding of VGAM128 RNA, herein designated VGAM RNA, to host target binding sites on VGAM128 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM128 host target RNA into VGAM128 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10057] It is appreciated that VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM128 host target genes. The mRNA of each one of this plurality of VGAM128 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM128 RNA, herein designated VGAM RNA, and which when bound by VGAM128 RNA causes inhibition of translation of respective one or more VGAM128 host target proteins.

[10058] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM128 gene, herein designated VGAM GENE, on one or more VGAM128 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10059] It is yet further appreciated that a function of VGAM128 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM128 correlate with, and may be deduced from, the identity of the host

target genes which VGAM128 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10060] Nucleotide sequences of the VGAM128 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM128 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM128 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM128 are further described hereinbelow with reference to Table 1.

[10061] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM128 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM128 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10062] As mentioned hereinabove with reference to Fig. 1, a function of VGAM128 gene, herein designated VGAM is inhibition of expression of VGAM128 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM128 correlate with, and may be deduced from, the identity of the target genes which VGAM128

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10063] Cyclin D2 (CCND2, Accession NM_001759) is a VGAM128 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7520, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10064] A function of VGAM128 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the G1/s (start) transition. Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 has been established by previous studies. Inaba et al. (1992) used murine cDNA clones for 3 cyclin D genes that are normally expressed during the G1 phase of the cell cycle to clone the cognate human genes. By analysis of somatic cell hybrids containing different human chro-

mosomes and by fluorescence in situ hybridization, they assigned the gene for cyclin D2 (CCND2) to 12p13. (Since the CCND1 gene (OMIM Ref. No. 168461) is on 11q13, this may be another bit of evidence of the homology of chromosomes 11 and 12.) Xiong et al. (1992) reported the cloning of the CCND2 gene and its assignment to 12p13 by fluorescence in situ hybridization. A pseudogene of CCND2 was mapped to 11q13 by Inaba et al. (1992). Kim et al. (2000) used Ccnd1- and Ccnd2-deficient mice to investigate the role of cyclins in Schwann cell growth. They concluded that neither Ccnd1 nor Ccnd2 is specifically required for the initial growth and maturation of Schwann cells during mouse development (see OMIM Ref. No. CCND1; 168461).

[10065] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10066] Inaba, T.; Matsushime, H.; Valentine, M.; Roussel, M. F.; Sherr, C. J.; Look, A. T. : Genomic organization, chromosomal localization, and independent expression of human cyclin D genes. *Genomics* 13: 565–574, 1992. ; and

[10067] Kim, H. A.; Pomeroy, S. L.; Whoriskey, W.; Pawlitzky, I.; Benowitz, L. I.; Sicinski, P.; Stiles, C. D.; Roberts, T. M. : A

developmentally regulated switch directs regenerative growth o.

[10068] Further studies establishing the function and utilities of CCND2 are found in John Hopkins OMIM database record ID 123833, and in cited publications numbered 4343–4345 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cerebellar Degeneration–related Protein 2, 62kDa (CDR2, Accession XM_071866) is another VGAM128 host target gene. CDR2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CDR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDR2 BINDING SITE, designated SEQ ID:37427, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10069] Another function of VGAM128 is therefore inhibition of Cerebellar Degeneration–related Protein 2, 62kDa (CDR2, Accession XM_071866), a gene which plays a role in cytokinesis, cell shape, and functions such as secretion and capping. Accordingly, utilities of VGAM128 include diag–

nosis, prevention and treatment of diseases and clinical conditions associated with CDR2. The function of CDR2 has been established by previous studies. Paraneoplastic cerebellar degeneration is an autoimmune disorder associated with neoplasms of lung, ovary, breast, or Hodgkin disease. Patients with paraneoplastic cerebellar degeneration carry a characteristic antibody called anti-Yo. On Western blot analysis of Purkinje cells and tumor tissue, the anti-Yo sera react with at least 2 antigens, a major species of 62 kD called CDR62 and a minor species of 34 kD called CDR34, where CDR means cerebellar degeneration-related. CDR34 is encoded by a gene on the X chromosome (CDR1; 302650). Furneaux et al. (1990) cloned and characterized the gene encoding CDR62, a leucine-zipper DNA-binding protein; see Fathallah-Shaykh et al. (1991). By a combination of study of rodent/human somatic cell hybrids and in situ hybridization, Gress et al. (1991, 1992) assigned the CDR2 gene to 16p13.1-p12. The gene is positioned in an interval that contains 2 rare heritable fragile sites. Fletcher et al. (1997) determined the mouse chromosomal locations of 9 genes that encode 'onconeural antigens,' i.e., antigens that are expressed by systemic tumors and elicit an immune response that

may develop into an autoimmune neuronal degeneration. One of these genes was the Cdr2 gene, which they mapped to mouse chromosome 7 in a region of homology to 16p13.1–p12.

[10070] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10071] Fathallah–Shaykh, H.; Wolf, S.; Wong, E.; Posner, J. B. : Cloning of a leucine–zipper protein recognized by the sera of patients with antibody–associated paraneoplastic cerebellar degeneration. Proc. Nat. Acad. Sci. 88: 3451–3454, 1991. ; and

[10072] Furneaux, H. M.; Rosenblum, M. K.; Dalmau, J.; Wong, E.; Woodruff, P.; Graus, F.; Posner, J. B. : Selective expression of Purkinje–cell antigens in tumor tissue from patients with parane.

[10073] Further studies establishing the function and utilities of CDR2 are found in John Hopkins OMIM database record ID 117340, and in cited publications numbered 12686, 10638–1063 and 12687–12688 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MAX Interacting Protein 1 (MXI1, Accession NM_005962) is another VGAM128 host target gene. MXI1

BINDING SITE1 and MXI1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MXI1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MXI1 BINDING SITE1 and MXI1 BINDING SITE2, designated SEQ ID:12586 and SEQ ID:28196 respectively, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10074] Another function of VGAM128 is therefore inhibition of MAX Interacting Protein 1 (MXI1, Accession NM_005962), a gene which acts as a tumor suppressor in vivo, engages the MYC network in a functionally relevant manner. Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MXI1. The function of MXI1 has been established by previous studies. One of the most common chromosomal abnormalities in prostate cancer involves loss of 10q22-qter. Rarely, a smaller deletion, involving 10q24-q25 has been observed, suggesting the presence of a tumor suppressor gene at that site. Prochownik et al. (1998) prospectively evaluated prostate tumors for loss of

MXI1 by FISH and cytogenetic techniques. Of 40 tumors, 21 (53%) demonstrated loss of a single MXI1 allele, as determined by FISH. In 10 cases with cytogenetically normal long arms of chromosome 10, but with FISH–documented deletion of MXI1, 8 mutations of MXI1 were identified. Five of the mutant proteins were incapable of binding DNA in association with MAX. Prochownik et al. (1998) concluded that MXI1 gene loss in prostate cancer is common and most frequently involves a cytogenetically undetectable deletion. Animal model experiments lend further support to the function of MXI1. MXI1 belongs to the family of proteins that function as potent antagonists of MYC oncoproteins. This antagonism relates to their ability to compete with MYC for the protein MAX and for consensus DNA binding sites and to recruit Sin3 proteins and their associated corepressors. Schreiber–Agus et al. (1998) disrupted the Mxi1 open reading frame in transgenic mice by eliminating an exon required for the production of the 2 mouse Mxi1 isoforms. They showed that the mice lacking Mxi1 exhibit progressive multisystem abnormalities. The mice also showed increased susceptibility to tumorigenesis either following carcinogen treatment or when also deficient in INK4A (OMIM Ref. No. 600160). This cancer–

prone phenotype may correspond with the enhanced ability of several MXI1-deficient cell types, including prostatic epithelium, to proliferate. The results show that MXI1 is involved in the homeostasis of differentiated organ systems, acts as a tumor suppressor in vivo, and engages the MYC network in a functionally relevant manner. In histologic studies of the mice, Schreiber-Agus et al. (1998) focused particularly on organs that normally express high or sustained levels of Mxi1, e.g., brain, spleen, kidney, and liver, and on tissue types that are susceptible to tumorigenesis when a putative tumor suppressor is lost from the 10q24-q26 region; for example, the spleen and thymus are susceptible to T-cell leukemia, the prostatic epithelium to prostate cancer, and the brain to glioblastoma multiforme when the 10q24-q26 region is mutated.

[10075] It is appreciated that the abovementioned animal model for MXI1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10076] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10077] Prochownik, E. V.; Grove, L. E.; Deubler, D.; Zhu, X. L.;

Stephenson, R. A.; Rohr, L. R.; Yin, X.; Brothman, A. R. :
Commonly occurring loss and mutation of the MXI1 gene
in prostate cancer. *Genes Chromosomes Cancer* 22:
295–304, 1998. ; and

[10078] Schreiber–Agus, N.; Meng, Y.; Hoang, T.; Hou, H., Jr.;
Chen, K.; Greenberg, R.; Cordon–Cardo, C.; Lee, H.–W.;
DePinho, R. A. : Role of Mxi1 in ageing organ systems and
the regulation of.

[10079] Further studies establishing the function and utilities of
MXI1 are found in John Hopkins OMIM database record ID
600020, and in cited publications numbered 8791, 8230,
8326–832 and 12617–8332 listed in the bibliography
section hereinbelow, which are also hereby incorporated
by reference. Stauf, RNA Binding Protein, Homolog 2
(Drosophila) (STAU2, Accession NM_014393) is another
VGAM128 host target gene. STAU2 BINDING SITE is HOST
TARGET binding site found in the 3` untranslated region
of mRNA encoded by STAU2, corresponding to a HOST
TARGET binding site such as BINDING SITE I, BINDING SITE
II or BINDING SITE III. Table 2 illustrates the complemen-
tarity of the nucleotide sequences of STAU2 BINDING SITE,
designated SEQ ID:15721, to the nucleotide sequence of
VGAM128 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2839.

[10080] Another function of VGAM128 is therefore inhibition of Staufen, RNA Binding Protein, Homolog 2 (Drosophila) (STAU2, Accession NM_014393). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAU2. ALDH9 (Accession NM_000696) is another VGAM128 host target gene. ALDH9 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ALDH9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH9 BINDING SITE, designated SEQ ID:6361, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10081] Another function of VGAM128 is therefore inhibition of ALDH9 (Accession NM_000696). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH9. FKSG44 (Accession NM_031904) is another VGAM128 host target gene. FKSG44 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA en-

coded by FKSG44, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FKSG44 BINDING SITE, designated SEQ ID:25649, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10082] Another function of VGAM128 is therefore inhibition of FKSG44 (Accession NM_031904). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FKSG44. FLJ20232 (Accession NM_019008) is another VGAM128 host target gene. FLJ20232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20232 BINDING SITE, designated SEQ ID:21086, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10083] Another function of VGAM128 is therefore inhibition of FLJ20232 (Accession NM_019008). Accordingly, utilities of

VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20232. GAPCENA (Accession NM_012197) is another VGAM128 host target gene. GAPCENA BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GAPCENA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAPCENA BINDING SITE, designated SEQ ID:14492, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10084] Another function of VGAM128 is therefore inhibition of GAPCENA (Accession NM_012197). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAPCENA. KIAA1040 (Accession XM_051091) is another VGAM128 host target gene. KIAA1040 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1040 BINDING SITE,

designated SEQ ID:35737, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10085] Another function of VGAM128 is therefore inhibition of KIAA1040 (Accession XM_051091). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1040. KIAA1165 (Accession XM_041162) is another VGAM128 host target gene. KIAA1165 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1165 BINDING SITE, designated SEQ ID:33473, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10086] Another function of VGAM128 is therefore inhibition of KIAA1165 (Accession XM_041162). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1165. KIAA1913 (Accession XM_058167) is another VGAM128 host target gene. KIAA1913 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1913, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1913 BINDING SITE, designated SEQ ID:36577, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10087] Another function of VGAM128 is therefore inhibition of KIAA1913 (Accession XM_058167). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1913. Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622) is another VGAM128 host target gene. MRPL35 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MRPL35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL35 BINDING SITE, designated SEQ ID:18738, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10088] Another function of VGAM128 is therefore inhibition of Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL35. Oxysterol Binding Protein-like 7 (OSBPL7, Accession NM_017731) is another VGAM128 host target gene. OSBPL7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OSBPL7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL7 BINDING SITE, designated SEQ ID:19318, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10089] Another function of VGAM128 is therefore inhibition of Oxysterol Binding Protein-like 7 (OSBPL7, Accession NM_017731). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL7. Septin 3 (SEPT3, Accession NM_019106) is another VGAM128 host target gene. SEPT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SEPT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT3 BINDING SITE, designated SEQ ID:21185, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10090] Another function of VGAM128 is therefore inhibition of Septin 3 (SEPT3, Accession NM_019106). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPT3. Solute Carrier Family 12 (potassium/chloride transporters), Member 8 (SLC12A8, Accession NM_024628) is another VGAM128 host target gene. SLC12A8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC12A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A8 BINDING SITE, designated SEQ ID:23894, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10091] Another function of VGAM128 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 8 (SLC12A8, Accession NM_024628). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A8. LOC115123 (Accession XM_055276) is another VGAM128 host target gene. LOC115123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115123 BINDING SITE, designated SEQ ID:36248, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10092] Another function of VGAM128 is therefore inhibition of LOC115123 (Accession XM_055276). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115123. LOC116028 (Accession XM_057225) is another VGAM128 host target gene. LOC116028 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC116028, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116028 BINDING SITE, designated SEQ ID:36493, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10093] Another function of VGAM128 is therefore inhibition of LOC116028 (Accession XM_057225). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116028. LOC122553 (Accession XM_058630) is another VGAM128 host target gene. LOC122553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122553 BINDING SITE, designated SEQ ID:36685, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10094] Another function of VGAM128 is therefore inhibition of LOC122553 (Accession XM_058630). Accordingly, utilities

of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122553. LOC145082 (Accession XM_096719) is another VGAM128 host target gene. LOC145082 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145082 BINDING SITE, designated SEQ ID:40494, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10095] Another function of VGAM128 is therefore inhibition of LOC145082 (Accession XM_096719). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145082. LOC145773 (Accession XM_085237) is another VGAM128 host target gene. LOC145773 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145773 BINDING SITE, designated SEQ ID:37985, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10096] Another function of VGAM128 is therefore inhibition of LOC145773 (Accession XM_085237). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145773. LOC146237 (Accession XM_096954) is another VGAM128 host target gene. LOC146237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146237 BINDING SITE, designated SEQ ID:40672, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10097] Another function of VGAM128 is therefore inhibition of LOC146237 (Accession XM_096954). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146237. LOC150319 (Accession XM_086816) is another VGAM128 host target gene. LOC150319 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150319 BINDING SITE, designated SEQ ID:38894, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10098] Another function of VGAM128 is therefore inhibition of LOC150319 (Accession XM_086816). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150319. LOC152348 (Accession XM_098204) is another VGAM128 host target gene. LOC152348 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152348 BINDING SITE, designated SEQ ID:41488, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10099] Another function of VGAM128 is therefore inhibition of

LOC152348 (Accession XM_098204). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152348. LOC201283 (Accession XM_017132) is another VGAM128 host target gene. LOC201283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201283 BINDING SITE, designated SEQ ID:30303, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10100] Another function of VGAM128 is therefore inhibition of LOC201283 (Accession XM_017132). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201283. LOC91397 (Accession XM_038219) is another VGAM128 host target gene. LOC91397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC91397 BINDING SITE, designated SEQ ID:32784, to the nucleotide sequence of VGAM128 RNA, herein designated VGAM RNA, also designated SEQ ID:2839.

[10101] Another function of VGAM128 is therefore inhibition of LOC91397 (Accession XM_038219). Accordingly, utilities of VGAM128 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91397. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 129 (VGAM129) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10102] VGAM129 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM129 was detected is described hereinabove with reference to Figs. 1–8.

[10103] VGAM129 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM129 host target gene, herein designated VGAM HOST TARGET GENE,

is a human gene contained in the human genome.

[10104] VGAM129 gene encodes a VGAM129 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM129 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM129 precursor RNA is designated SEQ ID:115, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:115 is located at position 285590 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10105] VGAM129 precursor RNA folds onto itself, forming VGAM129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10106] An enzyme complex designated DICER COMPLEX, `dices` the VGAM129 folded precursor RNA into VGAM129 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM129 RNA is designated SEQ ID:2840, and is provided hereinbelow with reference to the sequence listing part.

[10107] VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM129 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10108] VGAM129 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM129 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM129 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10109] The complementary binding of VGAM129 RNA, herein designated VGAM RNA, to host target binding sites on VGAM129 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM129 host target RNA into VGAM129 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[10110] It is appreciated that VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM129 host target genes. The mRNA of each one of this plurality of VGAM129 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM129 RNA, herein designated VGAM RNA, and which when bound by VGAM129 RNA causes inhibition of translation of respective one or more VGAM129 host target proteins.

[10111] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM129 gene, herein designated VGAM GENE, on one or more VGAM129 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10112] It is yet further appreciated that a function of VGAM129 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM129 correlate with, and may be deduced from, the identity of the host target genes which VGAM129 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10113] Nucleotide sequences of the VGAM129 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM129 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM129 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM129 are further described hereinbelow with reference to Table 1.

[10114] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM129 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM129 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10115] As mentioned hereinabove with reference to Fig. 1, a function of VGAM129 gene, herein designated VGAM is inhibition of expression of VGAM129 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM129 correlate with, and may be deduced from, the identity of the target genes which VGAM129 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10116] Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729) is a VGAM129 host target gene. DIAPH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIAPH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIAPH2 BINDING SITE, designated SEQ ID:13560, to the

nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, also designated SEQ ID:2840.

[10117] A function of VGAM129 is therefore inhibition of Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729), a gene which may affect in oogenesis. Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIAPH2. The function of DIAPH2 has been established by previous studies. Mutant alleles of Drosophila dia affect spermatogenesis or oogenesis and lead to sterility. Bione et al. (1998) characterized a human homolog of 'diaphanous' and demonstrated that this gene, designated DIA, is interrupted by a breakpoint in a patient with familial premature ovarian failure (POF; 311360). A human EST, DRES25, which showed significant homology with the Drosophila gene, was mapped to Xq22 by fluorescence in situ hybridization. Bione et al. (1998) found that the human DIA open reading frame encodes a 1,101-amino acid protein approximately 39% identical to the Drosophila protein. Northern blot analysis of human adult and fetal tissues detected 4 transcripts, 3 of which are expressed ubiquitously and the fourth exclusively in adult testis. Bione et al. (1998) showed that the DIA gene

is expressed in developing ovaries and testis of the mouse, as well as in all other tissues, from the E16 stage. Banfi et al. (1997) had indicated that a human homolog of 'diaphanous' maps to Xq22. Lynch et al. (1997) noted that a nonsyndromic form of X-linked deafness, DFN2 (OMIM Ref. No. 304500), also maps to Xq22, making this homologous gene a candidate for DFN2 hearing loss. In the family of patient BC studied by Sala et al. (1997), a balanced X;12 translocation, t(X;12)(q21;p1.3), was associated with premature ovarian failure (OMIM Ref. No. 311360). Patient BC had secondary amenorrhea, with no other associated features, at the age of 17 years. Her mother, who carried the same chromosomal rearrangement, was diagnosed with premature menopause at the age of 32 years. At diagnosis, both mother and daughter had high gonadotropin levels and inactivation of the normal X chromosome (Philippe et al., 1993). The breakpoint was mapped, by FISH, to a specific YAC. The translocation breakpoint was found to be in the last 200-kb intron of the gene.

[10118] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [10119] Bione, S.; Sala, C.; Manzini, C.; Arrigo, G.; Zuffardi, O.; Banfi, S.; Borsani, G.; Jonveaux, P.; Philippe, C.; Zuccotti, M.; Ballabio, A.; Toniolo, D. : A human homologue of the *Drosophila melanogaster* diaphanous gene is disrupted in a patient with premature ovarian failure: evidence for conserved function in oogenesis and implications for human sterility. *Am. J. Hum. Genet.* 62: 533–541, 1998. ; and
- [10120] Philippe, C.; Cremers, F. P. M.; Chery, M.; Bach, I.; Abbadi, N.; Ropers, H. H.; Gilgenkrantz, S. : Physical mapping of DNA markers in the q13–q22 region of the human X chromosome. *Genom.*
- [10121] Further studies establishing the function and utilities of DIAPH2 are found in John Hopkins OMIM database record ID 300108, and in cited publications numbered 9063, 9066, 906 and 9067 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB36, Member RAS Oncogene Family (RAB36, Accession NM_004914) is another VGAM129 host target gene. RAB36 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of RAB36 BINDING SITE, designated SEQ ID:11349, to the nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, also designated SEQ ID:2840.

[10122] Another function of VGAM129 is therefore inhibition of RAB36, Member RAS Oncogene Family (RAB36, Accession NM_004914), a gene which is involved in protein transport. Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB36. The function of RAB36 has been established by previous studies. Homozygous deletions at chromosome 22q11.2 are a recurrent cytogenetic characteristic of malignant rhabdoid tumors (MRTs), suggesting the presence of a tumor suppressor gene in this region. Mori et al. (1999) constructed a deletion map of the relevant part of 22q11.2 from a panel of 7 MRT cell lines, and isolated a novel gene from the center of the region. The gene, designated RAB36, spans approximately 19 kb of genomic DNA and contains 11 exons. It encodes a deduced 333-amino acid protein that contains 3 phosphate/magnesium-binding motifs, 3 guanine-binding motifs, a tyrosine kinase phosphorylation site, and a C-terminal isoprenylation signal. It shares high amino acid

sequence identity with mouse Rab23 (OMIM Ref. No. 606144) and human RAB13 (OMIM Ref. No. 602672). Northern blot analysis revealed 4.0- and 2.2-kb mRNAs in all human tissues examined. The larger transcript contains a longer 3-prime noncoding sequence. RT-PCR analysis revealed expression of RAB36 mRNAs in 1 MRT cell line and overexpression in 2 others. Direct sequencing of cDNA from these 3 cell lines showed neither nonsense nor frameshift mutations. Moreover, a colony-formation assay indicated that RAB36 is not concerned with cell proliferation or cell death. The authors thus concluded that RAB36 does not have a tumor suppressor function. Immunofluorescence studies localized RAB36 at the Golgi body, suggesting that RAB36, like some other Rab family proteins, is involved in vesicular transport around the Golgi apparatus. By use of exon trapping and large-scale genomic sequence analysis of 2 BAC clones, Zhou et al. (2000) also isolated RAB36, as well as another gene, RTDR1 (OMIM Ref. No. 605663), in the 22q11.2 region. They determined that RAB36 contains 11 exons. They also found no RAB36 mutations in rhabdoid tumor samples.

[10123] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [10124] Mori, T.; Fukuda, Y.; Kuroda, H.; Matsumura, T.; Ota, S.; Sugimoto, T.; Nakamura, Y.; Inazawa, J. : Cloning and characterization of a novel Rab-family gene, Rab36, within the region at 22q11.2 that is homozygously deleted in malignant rhabdoid tumors. *Biochem. Biophys. Res. Commun.* 254: 594–600, 1999. ; and
- [10125] Zhou, J.-Y.; Fogelgren, B.; Wang, Z.; Roe, B. A.; Biegel, J. A. : Isolation of genes from the rhabdoid tumor deletion region in chromosome band 22q11.2. *Gene* 241: 133–141, 2000.
- [10126] Further studies establishing the function and utilities of RAB36 are found in John Hopkins OMIM database record ID 605662, and in cited publications numbered 6412–6413 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sperm Associated Antigen 8 (SPAG8, Accession NM_012436) is another VGAM129 host target gene. SPAG8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPAG8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPAG8 BIND-

ING SITE, designated SEQ ID:14815, to the nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, also designated SEQ ID:2840.

[10127] Another function of VGAM129 is therefore inhibition of Sperm Associated Antigen 8 (SPAG8, Accession NM_012436), a gene which is a Sperm plasma membrane antigens are attractive antifertility vaccine targets. Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPAG8. The function of SPAG8 has been established by previous studies. Liu et al. (1996) obtained a full-length cDNA encoding SPAG8, which they termed SMP1. Sequence analysis predicted that the 523-amino acid type II transmembrane protein lacks a signal peptide but contains hydrophobic regions near the N and C termini that may function as transmembrane domains. Northern blot analysis detected a 2.45-kb transcript in testis. RT-PCR analysis revealed expression in testis but not in liver or kidney. Western blot analysis showed expression of a 55.5-kD protein, which is very similar to the predicted size. Immunofluorescence microscopy demonstrated expression in the acrosome of the sperm head. Using immunocytochemistry, Miao et al. (1995) found ex-

pression of SPAG8, which they called BS84 (84-kD Beijing sperm), in testis but not in brain, liver, or kidney. RNA dot blot hybridization analysis detected expression in testis but not in heart, brain, lung, or kidney. Autoradiographic analysis detected transcripts in spermatogonia, spermatocytes, and spermatid of seminiferous epithelium

[10128] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10129] Liu, Q.-Y.; Wang, L. F.; Miao, S. Y.; Catterall, J. F. : Expression and characterization of a novel human sperm membrane protein. Biol. Reprod. 54: 323-330, 1996. ; and

[10130] Miao, S.; Yan, Y.; Li, Y.; Bai, Y.; Wei, S.; Zong, C.; Zhao, M.; Zong, S.; Wang, L. : cDNA encoding a human sperm membrane protein BS-84. Prog. Natural Sci. 5: 119-122, 1995.

[10131] Further studies establishing the function and utilities of SPAG8 are found in John Hopkins OMIM database record ID 605731, and in cited publications numbered 6915-6917 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ZER6 (Accession XM_032742) is another VGAM129 host target gene. ZER6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

ZER6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZER6 BINDING SITE, designated SEQ ID:31740, to the nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, also designated SEQ ID:2840.

[10132] Another function of VGAM129 is therefore inhibition of ZER6 (Accession XM_032742). Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZER6. LOC205795 (Accession XM_120472) is another VGAM129 host target gene. LOC205795 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205795 BINDING SITE, designated SEQ ID:43610, to the nucleotide sequence of VGAM129 RNA, herein designated VGAM RNA, also designated SEQ ID:2840.

[10133] Another function of VGAM129 is therefore inhibition of LOC205795 (Accession XM_120472). Accordingly, utilities of VGAM129 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC205795. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 130 (VGAM130) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10134] VGAM130 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM130 was detected is described hereinabove with reference to Figs. 1–8.

[10135] VGAM130 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10136] VGAM130 gene encodes a VGAM130 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM130 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM130 precursor RNA is designated SEQ

ID:116, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:116 is located at position 99873 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10137] VGAM130 precursor RNA folds onto itself, forming VGAM130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10138] An enzyme complex designated DICER COMPLEX, `dices` the VGAM130 folded precursor RNA into VGAM130 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 56%) nucleotide sequence of VGAM130 RNA is designated SEQ ID:2841, and

is provided hereinbelow with reference to the sequence listing part.

[10139] VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM130 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[10140] VGAM130 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM130 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM130 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10141] The complementary binding of VGAM130 RNA, herein designated VGAM RNA, to host target binding sites on VGAM130 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM130 host target RNA into VGAM130 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10142] It is appreciated that VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM130 host target genes. The mRNA of each one of this plurality of VGAM130 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM130 RNA, herein designated VGAM RNA, and which when bound by VGAM130 RNA causes inhibition of translation of respective one or more VGAM130 host target proteins.

[10143] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM130 gene, herein designated VGAM GENE, on one or more VGAM130 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10144] It is yet further appreciated that a function of VGAM130 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM130 correlate with, and may be deduced from, the identity of the host target genes which VGAM130 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10145] Nucleotide sequences of the VGAM130 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM130 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM130 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM130 are further described hereinbelow with reference to Table 1.

[10146] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM130 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM130 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10147] As mentioned hereinabove with reference to Fig. 1, a function of VGAM130 gene, herein designated VGAM is inhibition of expression of VGAM130 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM130 correlate with, and may be deduced from, the identity of the target genes which VGAM130 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10148] Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome) (FGFR1, Accession NM_023107) is a VGAM130 host target gene. FGFR1 BINDING SITE1 and FGFR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGFR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGFR1 BINDING SITE1 and FGFR1 BINDING SITE2, designated SEQ ID:23364 and SEQ ID:23368 respectively, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10149] A function of VGAM130 is therefore inhibition of Fibroblast Growth Factor Receptor 1 (fms-related tyrosine kinase

2, Pfeiffer syndrome) (FGFR1, Accession NM_023107). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGFR1. AOP2 (Accession NM_004905) is another VGAM130 host target gene. AOP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AOP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AOP2 BINDING SITE, designated SEQ ID:11340, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10150] Another function of VGAM130 is therefore inhibition of AOP2 (Accession NM_004905). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AOP2. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728) is another VGAM130 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38832, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10151] Another function of VGAM130 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. SERP1 (Accession NM_014445) is another VGAM130 host target gene. SERP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERP1 BINDING SITE, designated SEQ ID:15798, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10152] Another function of VGAM130 is therefore inhibition of SERP1 (Accession NM_014445). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SERP1. Zinc Finger Protein 337 (ZNF337, Accession XM_042807) is another VGAM130 host target gene. ZNF337 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF337 BINDING SITE, designated SEQ ID:33771, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10153] Another function of VGAM130 is therefore inhibition of Zinc Finger Protein 337 (ZNF337, Accession XM_042807). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF337. LOC147077 (Accession XM_085699) is another VGAM130 host target gene. LOC147077 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC147077, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147077 BINDING SITE, desig-

nated SEQ ID:38294, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10154] Another function of VGAM130 is therefore inhibition of LOC147077 (Accession XM_085699). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147077. LOC200197 (Accession XM_114148) is another VGAM130 host target gene. LOC200197 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200197, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200197 BINDING SITE, designated SEQ ID:42733, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10155] Another function of VGAM130 is therefore inhibition of LOC200197 (Accession XM_114148). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200197. LOC253747 (Accession XM_173619) is another VGAM130 host target gene. LOC253747 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC253747, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253747 BINDING SITE, designated SEQ ID:46552, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10156] Another function of VGAM130 is therefore inhibition of LOC253747 (Accession XM_173619). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253747. LOC86651 (Accession XM_044052) is another VGAM130 host target gene. LOC86651 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC86651, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC86651 BINDING SITE, designated SEQ ID:34100, to the nucleotide sequence of VGAM130 RNA, herein designated VGAM RNA, also designated SEQ ID:2841.

[10157] Another function of VGAM130 is therefore inhibition of

LOC86651 (Accession XM_044052). Accordingly, utilities of VGAM130 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC86651. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 131 (VGAM131) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10158] VGAM131 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM131 was detected is described hereinabove with reference to Figs. 1–8.

[10159] VGAM131 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10160] VGAM131 gene encodes a VGAM131 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM131 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM131 precursor RNA is designated SEQ ID:117, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:117 is located at position 224021 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10161] VGAM131 precursor RNA folds onto itself, forming VGAM131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10162] An enzyme complex designated DICER COMPLEX, `dices` the VGAM131 folded precursor RNA into VGAM131 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 68%) nucleotide sequence of VGAM131 RNA is designated SEQ ID:2842, and is provided hereinbelow with reference to the sequence listing part.

[10163] VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM131 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[10164] VGAM131 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM131 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM131 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10165] The complementary binding of VGAM131 RNA, herein designated VGAM RNA, to host target binding sites on VGAM131 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM131 host target RNA into VGAM131 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10166] It is appreciated that VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM131 host target genes. The mRNA of each one of this plurality of VGAM131 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM131 RNA, herein designated VGAM RNA, and which when bound by VGAM131 RNA causes inhibition of translation of respective one or more VGAM131 host target proteins.

[10167] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM131 gene, herein designated VGAM GENE, on one or more VGAM131 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10168] It is yet further appreciated that a function of VGAM131 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM131 correlate with, and may be deduced from, the identity of the host target genes which VGAM131 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10169] Nucleotide sequences of the VGAM131 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM131 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM131 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM131 are further described hereinbelow with reference to Table 1.

[10170] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM131 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM131 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[10171] As mentioned hereinabove with reference to Fig. 1, a function of VGAM131 gene, herein designated VGAM is inhibition of expression of VGAM131 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM131 correlate with, and may be deduced from, the identity of the target genes which VGAM131 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10172] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139025) is a VGAM131 host target gene. ADAMTS13 BINDING SITE1 through ADAMTS13 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAMTS13, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS13 BINDING SITE1 through ADAMTS13 BINDING SITE3, designated SEQ ID:29124, SEQ ID:29126 and SEQ ID:29128 respectively, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2842.

[10173] A function of VGAM131 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 13 (ADAMTS13, Accession NM_139025), a gene which cleaves aggrecan, a cartilage proteoglycan, and may be involved in its turnover. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS13. The function of ADAMTS13 has been established by previous studies. Furlan et al. (1996) and Tsai (1996) independently reported that a metal-containing proteolytic enzyme (metalloprotease) in normal plasma cleaves the peptide bond between tyrosine at position 842 and methionine at position 843 in monomeric subunits of von Willebrand factor (VWF; 193400), thereby degrading the large multimers. This von Willebrand factor-cleaving protease was found by Furlan et al. (1997) to be deficient in 4 patients with chronic relapsing thrombotic thrombocytopenic purpura (OMIM Ref. No. 274150), 2 of whom were brothers. Because no inhibitor of the enzyme was detected in plasma, the deficiency was ascribed to an abnormality in the production, survival, or function of the protease. Furlan et al. (1998) studied plasma sam-

ples from 30 patients with thrombotic thrombocytopenic purpura and 23 patients with the hemolytic-uremic syndrome (HUS; 235400). Of 24 patients with nonfamilial thrombocytopenic purpura, 20 had severe and 4 had moderate protease deficiency during an acute event. An inhibitor of VWF found in 20 of the 24 patients (in all 5 plasma samples tested) was shown to be IgG, i.e., an antibody. Furlan et al. (1998) found that 6 patients with familial thrombocytopenic purpura lacked von Willebrand factor-cleaving protease activity but had no inhibitor, whereas all 10 patients with familial hemolytic-uremic syndrome had normal protease activity. In vitro proteolytic degradation of von Willebrand factor by the protease was studied in 5 patients with familial and 7 patients with nonfamilial hemolytic-uremic syndrome and was found to function normally in all 12 patients. In 2 Japanese families with Upshaw-Schulman syndrome (OMIM Ref. No. 276850), characterized by congenital TTP with neonatal onset and frequent relapses, Kokame et al. (2002) reported 4 novel mutations, 3 missense and 1 nonsense. Comparison of individual ADAMTS13 genotypes and plasma VWFCP activities indicated that 3 of the mutations, arg268 to pro (R268P; 604134.0014), gln449 to ter

(Q449X; 604134.0013), and cys508 to tyr (C508Y; 604134.0015), abrogated activity of the enzyme, whereas the fourth, pro475 to ser (P475S; 604134.0016), retained low but significant activity. The effects of these mutations were further confirmed by expression analysis in HeLa cells. Recombinant VWFCP containing either of the mutations R268P or C508Y was not secreted from cells; in contrast, VWFCP containing either Q449X or P475S was normally secreted but demonstrated minimal activity. Genotype analysis of 364 Japanese subjects revealed that the P475S mutation was heterozygous in 9.6% of individuals, suggesting that approximately 10% of the Japanese population possesses reduced VWFCP activity. Thus, the mutation represents an SNP associated with alterations in VWFCP activity that may be a risk factor for thrombotic disorders.

[10174] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10175] Furlan, M.; Robles, R.; Galbusera, M.; Remuzzi, G.; Kyrle, P. A.; Brenner, B.; Krause, M.; Scharrer, I.; Aumann, V.; Mittler, U.; Solenthaler, M.; Lammle, B. : Von Willebrand factor-cleaving protease in thrombotic thrombocytopenic

purpura and the hemolytic-uremic syndrome. New Eng. J. Med. 339: 1578-1584, 1998. ; and

[10176] Kokame, K.; Matsumoto, M.; Soejima, K.; Yagi, H.; Ishizashi, H.; Funato, M.; Tamai, H.; Konno, M.; Kamide, K.; Kawano, Y.; Miyata, T.; Fujimura, Y. : Mutations and common polymorphisms i.

[10177] Further studies establishing the function and utilities of ADAMTS13 are found in John Hopkins OMIM database record ID 604134, and in cited publications numbered 7412-7413, 9060-9061, 7414-741 and 6027-956 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Huntingtin (Huntington disease) (HD, Accession NM_002111) is another VGAM131 host target gene. HD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HD BINDING SITE, designated SEQ ID:7891, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10178] Another function of VGAM131 is therefore inhibition of

Huntingtin (Huntington disease) (HD, Accession NM_002111). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HD. LIM Domain Only 7 (LMO7, Accession NM_005358) is another VGAM131 host target gene. LMO7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LMO7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LMO7 BINDING SITE, designated SEQ ID:11826, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10179] Another function of VGAM131 is therefore inhibition of LIM Domain Only 7 (LMO7, Accession NM_005358). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LMO7. Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM_005898) is another VGAM131 host target gene. M11S1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by M11S1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of M11S1 BINDING SITE, designated SEQ ID:12517, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10180] Another function of VGAM131 is therefore inhibition of Membrane Component, Chromosome 11, Surface Marker 1 (M11S1, Accession NM_005898), a gene which may play a role in transporting nutrients from the gut lumen across the gutlining epithelial cell layer. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with M11S1. The function of M11S1 has been established by previous studies. The apical and basolateral borders of epithelial cells are distinguished by their different protein and lipid components. The sorting of newly synthesized membrane constituents to the appropriate region of the cell is accomplished either in the trans-Golgi network or by transcytosis, the selected transport of proteins to the appropriate surface. Transcytosis also is involved in the internalization of proteins and ligands at one surface and their transport to another. Ellis and Luzio (1995) identified a

protein which undergoes this process by raising antibodies against apical and basolateral membrane fractions prepared from the human intestinal cell line Caco-2 and treated with phosphatidylinositol-specific phospholipase C, an enzyme that cleaves glycosylphosphatidylinositol (GPI) linkages. The antibodies were then used to isolate cDNAs from a human colon carcinoma expression vector library. A composite cDNA sequence was determined that predicts a protein of 649 amino acids which migrates as a 137 kD homodimer; Ellis and Luzio (1995) designated the protein p137(GPI). The protein contains 3 distinct domains. The amino-terminal 275 residues contain several potential alpha helices, the middle region contains proline and glutamine-rich repeats, and residues 469-601 contain a potential GPI anchor site. Northern blots showed 3.4- and 2.7-kb transcripts in all tissues examined except for the testis, where 5.3- and 2.0-kb mRNAs were also observed. Ellis and Luzio (1995) showed that the protein was present at nearly equal amounts in both the apical and basolateral membranes of Caco-2 cells and that the protein appeared first at the basolateral side. Gessler et al. (1996) mapped the gene, designated M11S1, to 11p13 by virtue of their studies of CpG islands in contigs from

the region. The gene, which is adjacent to a CpG island, maps about 300 kb telomeric of CAT (OMIM Ref. No. 115500) and 200 kb centromeric to the LIM-domain only 2 gene (OMIM Ref. No. 180385). The order of transcription is telomere to centromere. Gessler et al. (1996) reported that mouse cDNA clones corresponding to the amino-terminal end of the protein showed that the human and mouse genes share greater than 97% sequence identity.

[10181] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10182] Ellis, J. A.; Luzio, J. P. : Identification and characterization of a novel protein (p137) which transcytoses bidirectionally in Caco-2 cells. J. Biol. Chem. 270: 20717-20723, 1995. ; and

[10183] Gessler, M.; Klamt, B.; Tsaoussidou, S.; Ellis, J. A.; Luzio, J. P. : The gene encoding the GPI-anchored membrane protein p137(GPI) (M11S1) maps to human chromosome 11p13 and is highly cons.

[10184] Further studies establishing the function and utilities of M11S1 are found in John Hopkins OMIM database record ID 601178, and in cited publications numbered

9318–9319 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphodiesterase 1A, Calmodulin-dependent (PDE1A, Accession NM_005019) is another VGAM131 host target gene. PDE1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PDE1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE1A BINDING SITE, designated SEQ ID:11457, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10185] Another function of VGAM131 is therefore inhibition of Phosphodiesterase 1A, Calmodulin-dependent (PDE1A, Accession NM_005019), a gene which is a Ca^{2+} -calmodulin dependent cyclic nucleotide phosphodiesterase and has a higher affinity for cGMP than for cAMP. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE1A. The function of PDE1A has been established by previous studies. Phosphodiesterase 1 is a membrane-bound exonuclease that hydrolyzes phospho-

diester bonds. See 171885. Wilson and McKenna (1988) examined the segregation of the gene for human phosphodiesterase 1A in human-rodent somatic cell hybrids. Electrophoretic analysis of phosphodiesterase 1A in hybrids suggested that the enzyme is a monomer. The PDE1A gene segregated concordantly with human chromosome 4 in all but 1 of 26 hybrids examined and showed 4 or more instances of discordance with all other chromosomes. By screening a hippocampus library with a bovine 61-kD CaM PDE cDNA, Loughney et al. (1996) isolated cDNAs encoding PDE1A (HCAM1) and PDE1C (HCAM3; 602987). The sequence of the predicted 535-amino acid protein is 94% identical to that of the bovine 61-kD CaM PDE when 2 short regions unique to PDE1A are excluded from comparison. Northern blot analysis revealed tissue-specific expression of 4.8-, 2.4-, and 2.6-kb PDE1A mRNAs, with transcripts most abundant in brain, heart, kidney, and skeletal muscle. Although expression of full-length PDE1A in *S. cerevisiae* did not result in PDE activity, an amino-truncated protein gave measurable PDE activity with higher affinity for cGMP than for cAMP.

[10186] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [10187] Loughney, K.; Martins, T. J.; Harris, E. A. S.; Sadhu, K.; Hicks, J. B.; Sonnenburg, W. K.; Beavo, J. A.; Ferguson, K. : Isolation and characterization of cDNAs corresponding to two human calcium, calmodulin-regulated, 3-prime,5-prime-cyclic nucleotide phosphodiesterases. J. Biol. Chem. 271: 796-806, 1996. ; and
- [10188] Wilson, D. E.; McKenna, L. : Assignment of the human gene for phosphodiesterase 1A to chromosome 4. (Abstract) Am. J. Hum. Genet. 43: A162 only, 1988.
- [10189] Further studies establishing the function and utilities of PDE1A are found in John Hopkins OMIM database record ID 171890, and in cited publications numbered 12446-12447 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pituitary Tumor-transforming 1 Interacting Protein (PTTG1IP, Accession NM_004339) is another VGAM131 host target gene. PTTG1IP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTTG1IP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PTTG1IP BINDING SITE, designated SEQ ID:10535, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10190] Another function of VGAM131 is therefore inhibition of Pituitary Tumor-transforming 1 Interacting Protein (PTTG1IP, Accession NM_004339), a gene which facilitates the translocation of PTTG to the nucleus. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTTG1IP. The function of PTTG1IP has been established by previous studies. In the course of constructing a transcript map for chromosome 21, Yaspo et al. (1995) isolated numerous coding segments from 21q22.3, including transcription unit TU6. Yaspo et al. (1998) cloned cDNAs corresponding to TU6 by screening a human fetal thymus cDNA library with a partial cDNA and trapped exon from TU6. Homology searches of sequence databases using the translated sequence did not detect similarities to known proteins, and the authors named the novel gene C21ORF3. The predicted 180-amino acid C21ORF3 protein has features of a type Ia integral membrane protein and contains the tetrapeptide YXRF, a motif

observed in proteins internalized via coated pit-mediated endocytosis. Northern blot analysis detected a 2.69-kb C21ORF3 mRNA in all tissues examined. Using a yeast 2-hybrid screen on a human testis cDNA library with rat pituitary tumor-transforming gene (PTTG; 604147) as bait, Chien and Pei (2000) isolated a cDNA encoding PTTG1IP, which they called PBF (PTTG-binding factor). Sequence analysis predicted that the 179-amino acid PBF protein, which is 92% identical to C21ORF3, contains multiple phosphorylation sites, 5 potential N- and O-glycosylation sites, a potential N-terminal sorting signal, and a C-terminal nuclear localization signal (NLS). Northern and dot blot analysis detected a 2.8-kb PBF transcript in all tissues tested, with highest expression in placenta. Pull-down and coimmunoprecipitation analyses showed that PBF and PTTG interact specifically via their C-terminal regions. Western blot analysis and immunofluorescence microscopy showed that whereas PTTG is expressed primarily in the cytoplasm, PBF is expressed in both the cytoplasm and nucleus. The authors demonstrated that PBF, via its NLS, facilitates the translocation of PTTG to the nucleus. Reporter assay analysis indicated that coexpression of PBF and PTTG induces transcription of basic fibroblast

growth factor (FGF2; 134920).

[10191] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10192] Yaspo, M.-L.; Aaltonen, J.; Horelli-Kuitunen, N.; Peltonen, L.; Lehrach, H. : Cloning of a novel human putative type Ia integral membrane protein mapping to 21q22.3. *Genomics* 49: 133–136, 1998. ; and

[10193] Yaspo, M.-L.; Gellen, L.; Mott, R.; Korn, B.; Nizetic, D.; Poustka, A. M.; Lehrach, H. : Model for a transcript map of human chromosome 21: isolation of new coding sequences from exon an.

[10194] Further studies establishing the function and utilities of PTTG1IP are found in John Hopkins OMIM database record ID 603784, and in cited publications numbered 8194–8196 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB36, Member RAS Oncogene Family (RAB36, Accession NM_004914) is another VGAM131 host target gene. RAB36 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAB36, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of RAB36 BINDING SITE, designated SEQ ID:11348, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10195] Another function of VGAM131 is therefore inhibition of RAB36, Member RAS Oncogene Family (RAB36, Accession NM_004914), a gene which is involved in protein transport. Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB36. The function of RAB36 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM129. Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242) is another VGAM131 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB2 BINDING SITE, designated SEQ ID:9238, to the nucleotide sequence

of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10196] Another function of VGAM131 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB2. 7h3 (Accession NM_033025) is another VGAM131 host target gene. 7h3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by 7h3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 7h3 BINDING SITE, designated SEQ ID:26915, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10197] Another function of VGAM131 is therefore inhibition of 7h3 (Accession NM_033025). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 7h3. DKFZp547C176 (Accession XM_040799) is another VGAM131 host target gene. DKFZp547C176 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547C176, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547C176 BINDING SITE, designated SEQ ID:33381, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10198] Another function of VGAM131 is therefore inhibition of DKFZp547C176 (Accession XM_040799). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547C176. DKFZp586I021 (Accession NM_032271) is another VGAM131 host target gene. DKFZp586I021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp586I021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586I021 BINDING SITE, designated SEQ ID:26019, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10199] Another function of VGAM131 is therefore inhibition of DKFZp586I021 (Accession NM_032271). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586I021. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295) is another VGAM131 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34936, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10200] Another function of VGAM131 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ10540 (Accession NM_018131) is another VGAM131 host target gene. FLJ10540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by FLJ10540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10540 BINDING SITE, designated SEQ ID:19927, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10201] Another function of VGAM131 is therefore inhibition of FLJ10540 (Accession NM_018131). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10540. H11 (Accession NM_014365) is another VGAM131 host target gene. H11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H11 BINDING SITE, designated SEQ ID:15691, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10202] Another function of VGAM131 is therefore inhibition of H11 (Accession NM_014365). Accordingly, utilities of

VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H11.

HYA22 (Accession NM_005808) is another VGAM131 host target gene. HYA22 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HYA22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYA22 BINDING SITE, designated SEQ ID:12387, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10203] Another function of VGAM131 is therefore inhibition of HYA22 (Accession NM_005808). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYA22. KIAA0553 (Accession XM_045981) is another VGAM131 host target gene. KIAA0553 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0553 BINDING SITE,

designated SEQ ID:34634, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10204] Another function of VGAM131 is therefore inhibition of KIAA0553 (Accession XM_045981). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0553. KIAA0828 (Accession XM_088105) is another VGAM131 host target gene. KIAA0828 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0828 BINDING SITE, designated SEQ ID:39510, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10205] Another function of VGAM131 is therefore inhibition of KIAA0828 (Accession XM_088105). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0828. KIAA1522 (Accession XM_036299) is another VGAM131 host target gene. KIAA1522 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1522 BINDING SITE, designated SEQ ID:32418, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10206] Another function of VGAM131 is therefore inhibition of KIAA1522 (Accession XM_036299). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1522. KIAA1560 (Accession XM_034422) is another VGAM131 host target gene. KIAA1560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1560 BINDING SITE, designated SEQ ID:32100, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10207] Another function of VGAM131 is therefore inhibition of KIAA1560 (Accession XM_034422). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1560. MGC13105 (Accession XM_049394) is another VGAM131 host target gene. MGC13105 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13105, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13105 BINDING SITE, designated SEQ ID:35406, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10208] Another function of VGAM131 is therefore inhibition of MGC13105 (Accession XM_049394). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13105. MGC32043 (Accession NM_144582) is another VGAM131 host target gene. MGC32043 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC32043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32043 BINDING SITE, designated SEQ ID:29392, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10209] Another function of VGAM131 is therefore inhibition of MGC32043 (Accession NM_144582). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC32043. Neuronal Pentraxin Receptor (NPTXR, Accession NM_058178) is another VGAM131 host target gene. NPTXR BINDING SITE1 and NPTXR BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NPTXR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPTXR BINDING SITE1 and NPTXR BINDING SITE2, designated SEQ ID:27736 and SEQ ID:15588 respectively, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10210] Another function of VGAM131 is therefore inhibition of Neuronal Pentraxin Receptor (NPTXR, Accession NM_058178). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPTXR. LOC149837 (Accession XM_097747) is another VGAM131 host target gene. LOC149837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC149837 BINDING SITE, designated SEQ ID:41097, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10211] Another function of VGAM131 is therefore inhibition of LOC149837 (Accession XM_097747). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149837. LOC150605 (Accession XM_097927) is another VGAM131 host target gene. LOC150605 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150605, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150605 BINDING SITE, designated SEQ ID:41231, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10212] Another function of VGAM131 is therefore inhibition of LOC150605 (Accession XM_097927). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150605. LOC155064 (Accession XM_088128) is an-

other VGAM131 host target gene. LOC155064 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155064 BINDING SITE, designated SEQ ID:39531, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10213] Another function of VGAM131 is therefore inhibition of LOC155064 (Accession XM_088128). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155064. LOC160156 (Accession XM_090047) is another VGAM131 host target gene. LOC160156 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC160156, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC160156 BINDING SITE, designated SEQ ID:39990, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10214] Another function of VGAM131 is therefore inhibition of LOC160156 (Accession XM_090047). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC160156. LOC197201 (Accession XM_113839) is another VGAM131 host target gene. LOC197201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197201 BINDING SITE, designated SEQ ID:42463, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10215] Another function of VGAM131 is therefore inhibition of LOC197201 (Accession XM_113839). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197201. LOC91960 (Accession XM_041872) is another VGAM131 host target gene. LOC91960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91960, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91960 BINDING SITE, designated SEQ ID:33608, to the nucleotide sequence of VGAM131 RNA, herein designated VGAM RNA, also designated SEQ ID:2842.

[10216] Another function of VGAM131 is therefore inhibition of LOC91960 (Accession XM_041872). Accordingly, utilities of VGAM131 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91960. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 132 (VGAM132) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10217] VGAM132 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM132 was detected is described hereinabove with reference to Figs. 1–8.

[10218] VGAM132 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM132 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10219] VGAM132 gene encodes a VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM132 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM132 precursor RNA is designated SEQ ID:118, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:118 is located at position 44993 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10220] VGAM132 precursor RNA folds onto itself, forming VGAM132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10221] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM132 folded precursor RNA into VGAM132 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM132 RNA is designated SEQ ID:2843, and is provided hereinbelow with reference to the sequence listing part.

[10222] VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM132 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10223] VGAM132 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM132 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM132 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10224] The complementary binding of VGAM132 RNA, herein designated VGAM RNA, to host target binding sites on VGAM132 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM132 host target RNA into VGAM132 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10225] It is appreciated that VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM132 host target genes. The mRNA of each one of this plurality of VGAM132 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM132 RNA, herein designated VGAM RNA, and which when bound by VGAM132 RNA causes inhibition of translation of respective one or more VGAM132 host target proteins.

[10226] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM132 gene, herein designated VGAM GENE, on one or more VGAM132 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10227] It is yet further appreciated that a function of VGAM132 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM132 correlate with, and may be deduced from, the identity of the host target genes which VGAM132 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10228] Nucleotide sequences of the VGAM132 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM132 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM132 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM132 are further

described hereinbelow with reference to Table 1.

[10229] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM132 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM132 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10230] As mentioned hereinabove with reference to Fig. 1, a function of VGAM132 gene, herein designated VGAM is inhibition of expression of VGAM132 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM132 correlate with, and may be deduced from, the identity of the target genes which VGAM132 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10231] G Protein-coupled Receptor 81 (GPR81, Accession NM_032554) is a VGAM132 host target gene. GPR81 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPR81, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of GPR81 BINDING SITE, designated SEQ ID:26280, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10232] A function of VGAM132 is therefore inhibition of G Protein-coupled Receptor 81 (GPR81, Accession NM_032554). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR81. Major Histocompatibility Complex, Class II, DQ Alpha 1 (HLA-DQA1, Accession XM_175260) is another VGAM132 host target gene. HLA-DQA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLA-DQA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLA-DQA1 BINDING SITE, designated SEQ ID:46724, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10233] Another function of VGAM132 is therefore inhibition of Major Histocompatibility Complex, Class II, DQ Alpha 1 (HLA-DQA1, Accession XM_175260), a gene which is alpha 1 chain of HLA-DQ1 class II molecule (Ia antigen)

which binds peptides and presents them to CD4+ T lymphocytes. Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLA-DQA1. The function of HLA-DQA1 has been established by previous studies. In multiple sclerosis patients, it showed the same frequency as in the normal population. Todd et al. (1987) presented a map of the class II loci. They suggested that the structure of the DQ molecule, in particular residue 57 of the beta-chain, specifies the autoimmune response against insulin-producing islet cells that leads to insulin-dependent diabetes mellitus (IDDM; 222100). Of the approximately 14 class II HLA genes within the HLA-D region, the DQ3.2-beta gene accounts for the well-documented association of HLA-DR4 with insulin-dependent diabetes mellitus and is the single allele most highly correlated with this disease. Kwok et al. (1989) found that amino acid 45 was critical for generating serologic epitopes characterizing the DQ3.2-beta gene and its nondiabetic allele, DQ3.1-beta. Todd et al. (1990) found that in Japanese, IDDM was more strongly associated with HLA-DQ than with HLA-DR; that the A3 allele at the DQA1 locus was most strongly associated with disease; that the

DQw8 allele of the DQB1 locus, which is associated with susceptibility to type I diabetes in Caucasians and Blacks, was not increased in frequency in Japanese patients; and that asp57–encoding DQB1 alleles, which are associated with reduced susceptibility to type I diabetes in Caucasians, was present in all except 1 of 49 Japanese patients and in all of 31 controls, in at least heterozygous state. Forty percent of patients were homozygous for asp57–encoding DQB1 alleles versus 35% of controls. The high frequency of asp57–encoding DQB1 alleles in Japanese may account for the rarity of type I diabetes in Japan. Animal model experiments lend further support to the function of HLA–DQA1. Studies supporting a role for HLA–DQ polymorphism in human rheumatoid arthritis were supported by Nabozny et al. (1996) and Bradley et al. (1997). Nabozny et al. (1996) demonstrated that mice transgenic for HLA–DQ8, a DQ allele associated with susceptibility to RA, developed severe arthritis after type II collagen immunization. Bradley et al. (1997) generated mice transgenic for HLA–DQ6, an allele associated with a nonsusceptible haplotype, and found that the DQ6 mice were resistant to collagen–induced arthritis. They also assessed the combined effect of an RA–susceptible and an

RA-nonassociated DQ allele by producing double-transgenic mice expressing both DQ6 and DQ8 molecules, representing the more prevalent condition found in humans where heterozygosity at the DQ allele is common. The double-transgenic mice developed moderate collagen-induced arthritis when immunized with type II collagen as compared with the severe arthritis observed in DQ8 transgenic mice, much like RA patients bearing both susceptible and nonsusceptible HLA haplotypes.

[10234] It is appreciated that the abovementioned animal model for HLA-DQA1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10235] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10236] Todd, J. A.; Fukui, Y.; Kitagawa, T.; Sasazuki, T. : The A3 allele of the HLA-DQA1 locus is associated with susceptibility to type 1 diabetes in Japanese. Proc. Nat. Acad. Sci. 87: 1094-1098, 1990. ; and

[10237] Bradley, D. S.; Nabozny, G. H.; Cheng, S.; Zhou, P.; Griffiths, M. M.; Luthra, H. S.; David, C. S. : HLA-DQB1 polymorphism determines incidence, onset, and severity of

collagen-induced a.

[10238] Further studies establishing the function and utilities of HLA-DQA1 are found in John Hopkins OMIM database record ID 146880, and in cited publications numbered 4206-113, 3296-126, 1144 and 288-293 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase Kinase Kinase 7 Interacting Protein 1 (MAP3K7IP1, Accession NM_006116) is another VGAM132 host target gene. MAP3K7IP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K7IP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K7IP1 BINDING SITE, designated SEQ ID:12762, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10239] Another function of VGAM132 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 7 Interacting Protein 1 (MAP3K7IP1, Accession NM_006116), a gene which may be an important signaling intermediate between tgfb receptors and map3k7/tak1. Accordingly,

utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K7IP1. The function of MAP3K7IP1 has been established by previous studies. Shibuya et al. (1996) used the yeast 2-hybrid system to identify brain cDNAs encoding proteins that interacted with TAK1 (OMIM Ref. No. 602614). They recovered a gene encoding a predicted 504-amino acid protein that they named TAB1 (TAK1-binding protein-1). On Northern blots, TAB1 was expressed as a 3.5-kb mRNA in all tissues tested Shibuya et al. (1996) found that in both yeast and mammalian cells, TAB1 activated the kinase activity of TAK1 by direct interaction. They showed that the C-terminal 68 amino acids of TAB1 are sufficient for binding and activation of TAK1 in mammalian cells, while the N-terminal 418 amino acids act as a dominant-negative inhibitor of transforming growth factor-beta (TGFB; 190180)-induced gene expression. Since TAK1 functions as an MAPKKK in the TGFB signaling pathway, Shibuya et al. (1996) suggested that TAB1 may be an important signaling intermediate between TGFB receptors and TAK1

[10240] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[10241] Shibuya, H.; Yamaguchi, K.; Shirakabe, K.; Tonegawa, A.; Gotoh, Y.; Ueno, N.; Irie, K.; Nishida, E.; Matsumoto, K. : TAB1: an activator of the TAK1 MAPKKK in TGF-beta signal transduction. Science 272: 1179-1182, 1996. ; and

[10242] Shibuya, H.; Yamaguchi, K.; Shirakabe, K.; Tonegawa, A.; Gotoh, Y.; Ueno, N.; Irie, K.; Nishida, E.; Matsumoto, K. : TAB1: an activator of the TAK1 MAPKKK in TGF-beta signal transduction. S.

[10243] Further studies establishing the function and utilities of MAP3K7IP1 are found in John Hopkins OMIM database record ID 602615, and in cited publications numbered 10124 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM_006165) is another VGAM132 host target gene. NFRKB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NFRKB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFRKB BINDING SITE, designated SEQ ID:12819, to the nucleotide sequence of VGAM132 RNA,

herein designated VGAM RNA, also designated SEQ ID:2843.

[10244] Another function of VGAM132 is therefore inhibition of Nuclear Factor Related to Kappa B Binding Protein (NFRKB, Accession NM_006165). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFRKB. PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746) is another VGAM132 host target gene. PCTK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCTK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCTK3 BINDING SITE, designated SEQ ID:36123, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10245] Another function of VGAM132 is therefore inhibition of PCTAIRE Protein Kinase 3 (PCTK3, Accession XM_053746), a gene which may play a role in signal transduction cascades in terminally differentiated cells. Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

PCTK3. The function of PCTK3 has been established by previous studies. The PCTAIRE protein kinases comprise a distinct subfamily of the CDC2 (OMIM Ref. No. 116940)-related serine/threonine-specific protein kinases. See PCTK1 (OMIM Ref. No. 311550). Meyerson et al. (1992) isolated a partial cDNA encoding PCTAIRE3. Like other members of the PCTAIRE subfamily, the predicted PCTAIRE3 protein contains an N-terminal extension relative to CDC2. The CDC2-related region of PCTAIRE3, excluding the N-terminal extension, shares 51%, 79%, and 80% protein sequence identity with CDC2, PCTK1, and PCTK2 (OMIM Ref. No. 603440), respectively. Northern blot analysis revealed that PCTAIRE3 is expressed in a variety of human cell lines and tissues. Okuda et al. (1992) identified the mouse homolog of PCTK3. By fluorescence in situ hybridization, Okuda et al. (1994) mapped the PCTK3 gene to 1q31-q32.

[10246] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10247] Meyerson, M.; Enders, G. H.; Wu, C.-L.; Su, L.-K.; Gorka, C.; Nelson, C.; Harlow, E.; Tsai, L.-H. : A family of human cdc2-related protein kinases. EMBO J. 11: 2909-2917,

1992. ; and

[10248] Okuda, T.; Cleveland, J. L.; Downing, J. R. : PCTAIRE-1 and PCTAIRE-3, two members of a novel cdc2/CDC28-related protein kinase gene family. *Oncogene* 7: 2249-2258, 1992.

[10249] Further studies establishing the function and utilities of PCK3 are found in John Hopkins OMIM database record ID 169190, and in cited publications numbered 15 and 3501-3502 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Paxillin (PXN, Accession NM_002859) is another VGAM132 host target gene. PXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXN BINDING SITE, designated SEQ ID:8755, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10250] Another function of VGAM132 is therefore inhibition of Paxillin (PXN, Accession NM_002859), a gene which may be involved in p53-dependent apoptosis. Accordingly, utilities of VGAM132 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with PXN. The function of PXN has been established by previous studies. *Drosophila* peroxidase is an extracellular matrix-associated peroxidase. It is expressed exclusively in hemocytes derived from head mesoderm at a very early stage of differentiation. Peroxidase exists as a homotrimer with a unique hybrid structure that combines an enzymatically functional peroxidase domain with motifs that are typically found in extracellular matrix-associated proteins. It is a secreted protein that contains a secretory recognition sequence at its N terminus. Peroxidase catalyzes hydrogen peroxide-driven radioiodination, oxidations, and the formation of dityrosine in vitro. It is also thought to function in extracellular matrix consolidation, phagocytosis, and defense. By sequencing random cDNAs corresponding to relatively long transcripts from the human immature myeloid cell line KG-1, Nagase et al. (1996) identified a cDNA, which they called KIAA0230, that encodes PRG2. The cDNA represents at least 90% of the full-length PRG2 transcript; however, since it lacks an inframe stop codon upstream of the first ATG, it may be missing 5-prime coding sequence. The 1,496-amino acid PRG2 protein deduced from the cDNA sequence contains

predicted transmembrane domains. PRG2 shares 38% amino acid sequence identity with *Drosophila* peroxidase across 1,412 amino acids. Northern blot analysis of human tissues showed PRG2 expression at higher levels in heart, lung, ovary, and placenta, and lower levels in liver, small intestine, colon, pancreas, spleen, kidney, thymus, skeletal muscle, testis, and prostate; PRG2 expression was not detected in brain or peripheral blood leukocytes.

[10251] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10252] Horikoshi, N.; Cong, J.; Kley, N.; Shenk, T. : Isolation of differentially expressed cDNAs from p53-dependent apoptotic cells: activation of the human homologue of the *Drosophila* peroxidase gene. *Biochem. Biophys. Res. Commun.* 261: 864–869, 1999. ; and

[10253] Nagase, T.; Seki, N.; Ishikawa, K.; Ohira, M.; Kawarabayashi, Y.; Ohara, O.; Tanaka, A.; Kotani, H.; Miyajima, N.; Nomura, N. : Prediction of the coding sequences of unidentified human g.

[10254] Further studies establishing the function and utilities of PXN are found in John Hopkins OMIM database record ID 605158, and in cited publications numbered 439 and

9379 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732) is another VGAM132 host target gene. RAD50 BINDING SITE1 and RAD50 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD50, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD50 BINDING SITE1 and RAD50 BINDING SITE2, designated SEQ ID:12294 and SEQ ID:28551 respectively, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10255] Another function of VGAM132 is therefore inhibition of RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732), a gene which is involved in dna double-strand break repair (dsbr). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD50. The function of RAD50 has been established by previous studies. The *S. cerevisiae* Rad50 gene encodes a protein that is essential for double-stranded DNA break repair by

nonhomologous DNA end joining and chromosomal integration. The yeast Rad50, Mre11 (OMIM Ref. No. 600814), and Xrs2 proteins appear to act in a multiprotein complex, consistent with the observation that mutations in these genes confer nearly identical phenotypes of no meiotic recombination and elevated rates of homologous mitotic recombination. By direct selection of cDNAs from the 5q23–q31 chromosomal interval, Dolganov et al. (1996) isolated a cDNA encoding a human Rad50 homolog. The human RAD50 gene spans 100 to 130 kb. Northern blot analysis revealed that the RAD50 gene was expressed as a 5.5–kb mRNA predominantly in testis. A faint 7–kb transcript, which the authors considered to be an mRNA with an alternatively processed 3–prime end, was also detected. Yeast Rad50 and the predicted 1,312–amino acid human RAD50 protein share more than 50% identity in their N– and C–termini. The central heptad repeat domains of the proteins have relatively divergent primary sequences but are predicted to adopt very similar coiled-coil structures. Using immunoprecipitation, Dolganov et al. (1996) demonstrated that the 153–kD RAD50 is stably associated with MRE11 in a protein complex, which may also include proteins of 95 kD, 200 kD, and 350 kD. By

inclusion within mapped clones and by analysis of somatic cell hybrids, Dolganov et al. (1996) mapped the RAD50 gene to 5q31. They suggested that a recombinational DNA repair deficiency may be associated with the development of myeloid leukemia, since this chromosomal region is frequently altered in acute myeloid leukemia and myelodysplastic disease.

[10256] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10257] Dolganov, G. M.; Maser, R. S.; Novikov, A.; Tosto, L.; Chong, S.; Bressan, D. A.; Petrini, J. H. J. : Human Rad50 is physically associated with human Mre11: identification of a conserved multiprotein complex implicated in recombinational DNA repair. *Molec. Cell Biol.* 16: 4832–4841, 1996. ; and

[10258] Hopfner, K.-P.; Craig, L.; Moncalian, G.; Zinkel, R. A.; Usui, T.; Owen, B. A. L.; Karcher, A.; Henderson, B.; Bodmer, J.-L.; McMurray, C. T.; Carney, J. P.; Petrini, J. H. J.; Tainer.

[10259] Further studies establishing the function and utilities of RAD50 are found in John Hopkins OMIM database record ID 604040, and in cited publications numbered 9233–8204, 7143, 8205, 820 and 7145–7146 listed in

the bibliography section hereinbelow, which are also hereby incorporated by reference. CXYorf1 (Accession XM_088704) is another VGAM132 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39904, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10260] Another function of VGAM132 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. FLJ00060 (Accession XM_028154) is another VGAM132 host target gene. FLJ00060 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ00060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00060 BINDING SITE,

designated SEQ ID:30628, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10261] Another function of VGAM132 is therefore inhibition of FLJ00060 (Accession XM_028154). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00060. FLJ10244 (Accession NM_018037) is another VGAM132 host target gene. FLJ10244 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10244, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10244 BINDING SITE, designated SEQ ID:19779, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10262] Another function of VGAM132 is therefore inhibition of FLJ10244 (Accession NM_018037). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10244. FLJ20257 (Accession NM_019606) is another VGAM132 host target gene. FLJ20257 BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by FLJ20257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20257 BINDING SITE, designated SEQ ID:21220, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10263] Another function of VGAM132 is therefore inhibition of FLJ20257 (Accession NM_019606). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20257. FLJ31951 (Accession NM_144726) is another VGAM132 host target gene. FLJ31951 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31951 BINDING SITE, designated SEQ ID:29550, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10264] Another function of VGAM132 is therefore inhibition of

FLJ31951 (Accession NM_144726). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31951. KIAA1001 (Accession NM_014960) is another VGAM132 host target gene. KIAA1001 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1001 BINDING SITE, designated SEQ ID:17325, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10265] Another function of VGAM132 is therefore inhibition of KIAA1001 (Accession NM_014960). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1001. KIAA1321 (Accession XM_030856) is another VGAM132 host target gene. KIAA1321 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1321, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1321 BINDING SITE, designated SEQ ID:31192, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10266] Another function of VGAM132 is therefore inhibition of KIAA1321 (Accession XM_030856). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1321. PRO2435 (Accession NM_018527) is another VGAM132 host target gene. PRO2435 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO2435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2435 BINDING SITE, designated SEQ ID:20600, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10267] Another function of VGAM132 is therefore inhibition of PRO2435 (Accession NM_018527). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO2435. Proline Rich 2 (PROL2, Accession NM_006813) is another

VGAM132 host target gene. PROL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PROL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PROL2 BINDING SITE, designated SEQ ID:13684, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10268] Another function of VGAM132 is therefore inhibition of Proline Rich 2 (PROL2, Accession NM_006813). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PROL2. Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215) is another VGAM132 host target gene. TGOLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGOLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGOLN2 BINDING SITE, designated SEQ ID:32022, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ

ID:2843.

[10269] Another function of VGAM132 is therefore inhibition of Trans-golgi Network Protein 2 (TGOLN2, Accession XM_034215). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGOLN2. LOC126917 (Accession XM_059091) is another VGAM132 host target gene. LOC126917 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126917 BINDING SITE, designated SEQ ID:36867, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10270] Another function of VGAM132 is therefore inhibition of LOC126917 (Accession XM_059091). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126917. LOC144866 (Accession XM_096699) is another VGAM132 host target gene. LOC144866 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC144866, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144866 BINDING SITE, designated SEQ ID:40479, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10271] Another function of VGAM132 is therefore inhibition of LOC144866 (Accession XM_096699). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144866. LOC145739 (Accession XM_085222) is another VGAM132 host target gene. LOC145739 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145739 BINDING SITE, designated SEQ ID:37962, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10272] Another function of VGAM132 is therefore inhibition of LOC145739 (Accession XM_085222). Accordingly, utilities

of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145739. LOC146287 (Accession XM_096967) is another VGAM132 host target gene. LOC146287 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146287, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146287 BINDING SITE, designated SEQ ID:40691, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10273] Another function of VGAM132 is therefore inhibition of LOC146287 (Accession XM_096967). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146287. LOC149842 (Accession XM_097745) is another VGAM132 host target gene. LOC149842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC149842 BINDING SITE, designated SEQ ID:41090, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10274] Another function of VGAM132 is therefore inhibition of LOC149842 (Accession XM_097745). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149842. LOC150951 (Accession XM_097975) is another VGAM132 host target gene. LOC150951 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150951 BINDING SITE, designated SEQ ID:41277, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10275] Another function of VGAM132 is therefore inhibition of LOC150951 (Accession XM_097975). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150951. LOC153277 (Accession XM_098346) is another VGAM132 host target gene. LOC153277 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153277 BINDING SITE, designated SEQ ID:41604, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10276] Another function of VGAM132 is therefore inhibition of LOC153277 (Accession XM_098346). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153277. LOC153727 (Accession XM_098422) is another VGAM132 host target gene. LOC153727 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153727 BINDING SITE, designated SEQ ID:41680, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10277] Another function of VGAM132 is therefore inhibition of

LOC153727 (Accession XM_098422). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153727. LOC220883 (Accession XM_166076) is another VGAM132 host target gene. LOC220883 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220883 BINDING SITE, designated SEQ ID:43849, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10278] Another function of VGAM132 is therefore inhibition of LOC220883 (Accession XM_166076). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220883. LOC221662 (Accession XM_166466) is another VGAM132 host target gene. LOC221662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC221662 BINDING SITE, designated SEQ ID:44387, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10279] Another function of VGAM132 is therefore inhibition of LOC221662 (Accession XM_166466). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221662. LOC257484 (Accession XM_114232) is another VGAM132 host target gene. LOC257484 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257484, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257484 BINDING SITE, designated SEQ ID:42813, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10280] Another function of VGAM132 is therefore inhibition of LOC257484 (Accession XM_114232). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257484. LOC92539 (Accession XM_045632) is an-

other VGAM132 host target gene. LOC92539 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC92539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92539 BINDING SITE, designated SEQ ID:34499, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10281] Another function of VGAM132 is therefore inhibition of LOC92539 (Accession XM_045632). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92539. LOC92719 (Accession XM_046853) is another VGAM132 host target gene. LOC92719 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92719 BINDING SITE, designated SEQ ID:34848, to the nucleotide sequence of VGAM132 RNA, herein designated VGAM RNA, also designated SEQ ID:2843.

[10282] Another function of VGAM132 is therefore inhibition of LOC92719 (Accession XM_046853). Accordingly, utilities of VGAM132 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92719. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 133 (VGAM133) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10283] VGAM133 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM133 was detected is described hereinabove with reference to Figs. 1–8.

[10284] VGAM133 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10285] VGAM133 gene encodes a VGAM133 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM133

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM133 precursor RNA is designated SEQ ID:119, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:119 is located at position 95821 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10286] VGAM133 precursor RNA folds onto itself, forming VGAM133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10287] An enzyme complex designated DICER COMPLEX, `dices` the VGAM133 folded precursor RNA into VGAM133 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM133 RNA is designated SEQ ID:2844, and is provided hereinbelow with reference to the sequence listing part.

[10288] VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM133 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10289] VGAM133 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM133 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM133 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10290] The complementary binding of VGAM133 RNA, herein designated VGAM RNA, to host target binding sites on VGAM133 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM133 host target RNA into VGAM133 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10291] It is appreciated that VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM133 host target genes. The mRNA of

each one of this plurality of VGAM133 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM133 RNA, herein designated VGAM RNA, and which when bound by VGAM133 RNA causes inhibition of translation of respective one or more VGAM133 host target proteins.

[10292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM133 gene, herein designated VGAM GENE, on one or more VGAM133 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[10293] It is yet further appreciated that a function of VGAM133 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM133 correlate with, and may be deduced from, the identity of the host target genes which VGAM133 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10294] Nucleotide sequences of the VGAM133 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM133 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM133 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM133 are further described hereinbelow with reference to Table 1.

[10295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM133 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM133 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10296] As mentioned hereinabove with reference to Fig. 1, a function of VGAM133 gene, herein designated VGAM is inhibition of expression of VGAM133 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM133 correlate with, and may be deduced from, the identity of the target genes which VGAM133 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10297] Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession NM_004423) is a VGAM133 host target gene. DVL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DVL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DVL3 BINDING SITE, designated SEQ ID:10690, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10298] A function of VGAM133 is therefore inhibition of Dishevelled, Dsh Homolog 3 (Drosophila) (DVL3, Accession

NM_004423), a gene which regulates cell proliferation. Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DVL3. The function of DVL3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Natural Killer-tumor Recognition Sequence (NKTR, Accession NM_005385) is another VGAM133 host target gene. NKTR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NKTR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NKTR BINDING SITE, designated SEQ ID:11862, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10299] Another function of VGAM133 is therefore inhibition of Natural Killer-tumor Recognition Sequence (NKTR, Accession NM_005385), a gene which is involved in the function of nk cells. Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NKTR. The function of NKTR

has been established by previous studies. The natural killer triggering receptor (NKTR) is involved in the recognition of tumor cells by large granular lymphocytes (LGLs) (Frey et al., 1991; Anderson et al., 1993). LGLs are a subpopulation of white blood cells that have the ability to kill target tumor cells by an MHC-independent mechanism. The protein product of the NKTR gene is present on the surface of LGLs and facilitates their binding to tumor targets. The gene codes for a protein of 150,000 Da, with a unique amino acid structure consisting of a 58-amino acid hydrophobic amino terminus followed by a cyclophilin-related domain. No other known mammalian receptor gene has been found to contain this strong identity to the cyclophilin protein in an external domain. By somatic cell hybrid analysis, Young et al. (1993) assigned the NKTR gene to 3p23-p21. Interspecific backcross analysis demonstrated that the murine homolog maps to the distal end of mouse chromosome 9 and is closely linked to the locus coding for cholecystokinin (Cck). This region of mouse 9 shares a region of homology with human 3p. Hybridization to DNA from a variety of species including the monkey, cat, and dog was observed, indicating that this gene is highly conserved among mammalian species.

Rinfret and Anderson (1993) observed 2 alternative splicing events in the 5-prime region of the NKTR mRNA in human and mouse. One uses an alternative exon 6 that disrupts the NKTR coding region and produces an mRNA encoding a truncated protein. The other splicing event generates a deletion by use of an alternative splice acceptor within exon 9. Rinfret and Anderson (1993) observed all 4 possible combinations of these events in cDNAs. Activation of natural killer cells by IL2 (OMIM Ref. No. 147680) changes the pattern of splicing, resulting in increased production of full-length protein. Simons-Evelyn et al. (1997) characterized the first 8 exons and 5-prime region of mouse Nktr. They found that mouse intron 5 also contains the alternative exon that disrupts the open reading frame.

[10300] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10301] Anderson, S. K.; Gallinger, S.; Roder, J.; Frey, J.; Young, H. A.; Ortaldo, J. R. : A cyclophilin-related protein involved in the function of natural killer cells. Proc. Nat. Acad. Sci. 90: 542-546, 1993. ; and

[10302] Rinfret, A.; Anderson, S. K. : IL-2 regulates the expression

of the NK-TR gene via an alternate RNA splicing mechanism. Molec. Immun. 30: 1307-1313, 1993.

[10303] Further studies establishing the function and utilities of NKTR are found in John Hopkins OMIM database record ID 161565, and in cited publications numbered 12732-12736 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prostaglandin E Receptor 2 (subtype EP2), 53kDa (PTGER2, Accession NM_000956) is another VGAM133 host target gene. PTGER2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGER2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGER2 BINDING SITE, designated SEQ ID:6659, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10304] Another function of VGAM133 is therefore inhibition of Prostaglandin E Receptor 2 (subtype EP2), 53kDa (PTGER2, Accession NM_000956), a gene which is a receptor for prostaglandin e2 mediating by g-s proteins that stimulates adenylate cyclase. Accordingly, utilities of VGAM133

include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGER2. The function of PTGER2 has been established by previous studies. Epithelial tumors may be regulated by cyclooxygenase (COX) enzyme products. To determine if COX2 (OMIM Ref. No. 600262) expression and PGE2 synthesis are upregulated in cervical cancers, Sales et al. (2001) used real-time quantitative PCR and Western blot analysis to confirm COX2 RNA and protein expression in squamous cell carcinomas and adenocarcinomas. In contrast, minimal expression of COX2 was detected in histologically normal cervix. Immunohistochemical analyses localized COX2 expression and PGE2 synthesis to neoplastic epithelial cells of all squamous cell carcinomas and adenocarcinomas studied. Immunoreactive COX2 and PGE2 were also colocalized to endothelial cells lining the microvasculature. To establish whether PGE2 has an autocrine/paracrine effect in cervical carcinomas, the authors investigated the expression of 2 subtypes of PGE2 receptors, namely EP2 and EP4 by real-time quantitative PCR. Expression of EP2 and EP4 receptors was significantly higher in carcinoma tissue than in histologically normal cervix. The authors concluded that COX2, EP2, and EP4 expression and PGE2 syn-

thesis are upregulated in cervical cancer tissue and that PGE₂ may regulate neoplastic cell function in cervical carcinoma in an autocrine/paracrine manner via the EP₂/EP₄ receptors. Animal model experiments lend further support to the function of PTGER₂. Using mice deficient in the prostaglandin EP₂ receptor, Tilley et al. (1999) showed that Ep₂ ^{-/-} females are infertile secondary to failure of the released ovum to become fertilized in vivo. Ep₂ ^{-/-} ova could be fertilized in vitro, suggesting that in addition to previously defined roles, prostaglandins may contribute to the microenvironment in which fertilization takes place. Besides its effects on reproduction, PGE₂ regulates regional blood flow in various vascular beds. Mice deficient in the EP₂ PGE₂ receptor displayed resting systolic blood pressure that was significantly lower than that in wildtype controls. Blood pressure increased in these animals when they were placed on a high salt diet, suggesting that the EP₂ receptor may be involved in sodium handling by the kidney.

[10305] It is appreciated that the abovementioned animal model for PTGER₂ is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

- [10306] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [10307] Tilley, S. L.; Audoly, L. P.; Hicks, E. H.; Kim, H.-S.; Flannery, P. J.; Coffman, T. M.; Koller, B. H. : Reproductive failure and reduced blood pressure in mice lacking the EP2 prostaglandin E-2 receptor. *J. Clin. Invest.* 103: 1539-1545, 1999. ; and
- [10308] Sales, K. J.; Katz, A. A.; Davis, M.; Hinz, S.; Soeters, R. P.; Hofmeyr, M. D.; Millar, R. P.; Jabbour, H. N. : Cyclooxygenase-2 expression and prostaglandin E2 synthesis are up-regulated.
- [10309] Further studies establishing the function and utilities of PTGER2 are found in John Hopkins OMIM database record ID 176804, and in cited publications numbered 1083 and 10841-10844 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Apoptosis Inhibitor 5 (API5, Accession NM_006595) is another VGAM133 host target gene. API5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by API5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of API5 BINDING SITE, designated SEQ ID:13361, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10310] Another function of VGAM133 is therefore inhibition of Apoptosis Inhibitor 5 (API5, Accession NM_006595). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with API5. FLJ12800 (Accession NM_022903) is another VGAM133 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800 BINDING SITE, designated SEQ ID:23189, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10311] Another function of VGAM133 is therefore inhibition of FLJ12800 (Accession NM_022903). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ14600 (Accession NM_032810) is another VGAM133

host target gene. FLJ14600 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14600, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14600 BINDING SITE, designated SEQ ID:26574, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10312] Another function of VGAM133 is therefore inhibition of FLJ14600 (Accession NM_032810). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14600. HERV-H LTR-associating 2 (HHLA2, Accession NM_007072) is another VGAM133 host target gene. HHLA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HHLA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HHLA2 BINDING SITE, designated SEQ ID:13937, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ

ID:2844.

[10313] Another function of VGAM133 is therefore inhibition of HERV-H LTR-associating 2 (HHLA2, Accession NM_007072). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HHLA2. LOC146227 (Accession XM_085374) is another VGAM133 host target gene. LOC146227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146227 BINDING SITE, designated SEQ ID:38082, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10314] Another function of VGAM133 is therefore inhibition of LOC146227 (Accession XM_085374). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146227. LOC170063 (Accession XM_104820) is another VGAM133 host target gene. LOC170063 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC170063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170063 BINDING SITE, designated SEQ ID:42186, to the nucleotide sequence of VGAM133 RNA, herein designated VGAM RNA, also designated SEQ ID:2844.

[10315] Another function of VGAM133 is therefore inhibition of LOC170063 (Accession XM_104820). Accordingly, utilities of VGAM133 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170063. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 134 (VGAM134) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10316] VGAM134 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM134 was detected is described hereinabove with reference to Figs. 1–8.

[10317] VGAM134 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10318] VGAM134 gene encodes a VGAM134 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM134 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM134 precursor RNA is designated SEQ ID:120, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:120 is located at position 80787 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10319] VGAM134 precursor RNA folds onto itself, forming VGAM134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[10320] An enzyme complex designated DICER COMPLEX, `dices` the VGAM134 folded precursor RNA into VGAM134 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM134 RNA is designated SEQ ID:2845, and is provided hereinbelow with reference to the sequence listing part.

[10321] VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM134 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10322] VGAM134 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM134 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM134 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM134 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10323] The complementary binding of VGAM134 RNA, herein designated VGAM RNA, to host target binding sites on VGAM134 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM134 host target RNA into VGAM134 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10324] It is appreciated that VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM134 host target genes. The mRNA of each one of this plurality of VGAM134 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM134 RNA, herein designated VGAM RNA, and which when bound by VGAM134 RNA causes inhibition of translation of respective one or more VGAM134 host target proteins.

[10325] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM134 gene, herein designated VGAM GENE, on one or more VGAM134 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10326] It is yet further appreciated that a function of VGAM134 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM134 correlate with, and may be deduced from, the identity of the host target genes which VGAM134 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10327] Nucleotide sequences of the VGAM134 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM134 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM134 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM134 are further described hereinbelow with reference to Table 1.

[10328] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM134 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM134 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10329] As mentioned hereinabove with reference to Fig. 1, a function of VGAM134 gene, herein designated VGAM is inhibition of expression of VGAM134 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM134 correlate with, and may be deduced from, the identity of the target genes which VGAM134 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10330] Interleukin 10 Receptor, Alpha (IL10RA, Accession XM_006447) is a VGAM134 host target gene. IL10RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL10RA, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL10RA BINDING SITE, designated SEQ ID:29998, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10331] A function of VGAM134 is therefore inhibition of Interleukin 10 Receptor, Alpha (IL10RA, Accession XM_006447), a gene which is a receptor for il-10. Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL10RA. The function of IL10RA has been established by previous studies. Interleukin-10 (OMIM Ref. No. 124092) is a cytokine produced by B cells, T helper cells, and cells of the monocyte/macrophage lineage that exhibits diverse activities on different cell lines. Tan et al. (1993) showed that the protein can be enzymatically iodinated to high specific radioactivity with retention of biologic activity. The radiolabeled ligand was found to bind specifically to its receptor in several mouse and human cell lines. For both mouse and human cell lines examined, there appeared to be at most only a few hundred IL10 receptors per cell. Mouse IL10 was capable of blocking binding of human IL10 to mouse but not human cells. Ho

et al. (1993) found that mouse il-10r is structurally related to interferon receptors. Since IL-10 inhibits macrophage activation by interferon-gamma, a possible implication of this relationship is interaction of IL-10R and IFN-gamma-R or their signaling pathways. Liu et al. (1994) assigned the IL10R gene to chromosome 11 by analysis of DNAs from human/hamster hybrid cell lines. Taniyama et al. (1995) regionalized the assignment to 11q23.3 by fluorescence in situ hybridization.

[10332] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10333] Ho, A. S. Y.; Liu, Y.; Khan, T. A.; Hsu, D.-H.; Bazan, J. F.; Moore, K. W. : A receptor for interleukin 10 is related to interferon receptors. Proc. Nat. Acad. Sci. 90: 11267-11271, 1993. ; and

[10334] Liu, Y.; Wei, S. H.-Y.; Ho, A. S.-Y.; de Waal Malefyt, R.; Moore, K. W. : Expression cloning and characterization of a human Il-10 receptor. J. Immun. 152: 1821-1829, 1994.

[10335] Further studies establishing the function and utilities of IL10RA are found in John Hopkins OMIM database record ID 146933, and in cited publications numbered

12525–12526, 88 and 2732 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. inositol(myo)–1(or 4)–monophosphatase 1 (IMPA1, Accession NM_005536) is another VGAM134 host target gene. IMPA1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IMPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMPA1 BINDING SITE, designated SEQ ID:12056, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10336] Another function of VGAM134 is therefore inhibition of inositol(myo)–1(or 4)–monophosphatase 1 (IMPA1, Accession NM_005536), a gene which is responsible for the provision of inositol required for synthesis of phosphatidylinositol and polyphosphoinositides. Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMPA1. The function of IMPA1 has been established by previous studies. Manic depressive illness (OMIM Ref. No. 125480) is a serious psychiatric disorder that in many,

but far from all, patients can be treated with lithium. The main causes for discontinuation of lithium therapy are unpleasant or serious side effects and lack of response. The reason for the striking variation in clinical efficacy of lithium treatment among bipolar patients is not known. The enzyme myo-inositol monophosphatase (OMIM Ref. No. IMPase) has been postulated as a target for the mood-stabilizing effects of lithium. The gene encoding human IMPase (IMPA1) was cloned by McAllister et al. (1992); variation in the 277-codon coding region of IMPA1 has not been observed in manic-depressive patients (Steen et al., 1996). It is nevertheless conceivable that polymorphisms or mutations in the noncoding regions of this gene could influence the lithium response in psychiatric patients. As a first step in investigating this possibility, Sjöholt et al. (1997) determined the genomic structure of the human IMPA1 gene. They found that it is composed of at least 9 exons and covers more than 20 kb of sequence on 8q21.13-q21.3. The chromosomal mapping was performed by PCR analysis of both CEPH megabase-insert YAC DNA pools and human/rodent somatic cell hybrid DNAs. In the 3-prime untranslated part of the gene, they observed a polymorphism (a G to A transition) and also 2

short sequences similar to the inositol/cholin-responsive element consensus. They postulated that 2 additional IMPA-like transcripts originate from the human genome, one from a position close to IMPA1 itself on chromosome 8 and the other from 18p

[10337] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10338] Sjholt, G.; Molven, A.; Lovlie, R.; Wilcox, A.; Sikela, J. M.; Steen, V. M. : Genomic structure and chromosomal localization of a human myo-inositol monophosphatase gene (IMPA). *Genomics* 45: 113–122, 1997. ; and

[10339] Steen, V. M.; Gulbrandsen, A. K.; Eiken, H. G.; Berle, J. O. : Lack of genetic variation in the coding region of the myo-inositol monophosphatase gene in lithium-treated patients with ma.

[10340] Further studies establishing the function and utilities of IMPA1 are found in John Hopkins OMIM database record ID 602064, and in cited publications numbered 8905–8907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ribosomal Protein L17 (RPL17, Accession NM_000985) is another VGAM134 host target gene. RPL17

BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RPL17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPL17 BINDING SITE, designated SEQ ID:6696, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10341] Another function of VGAM134 is therefore inhibition of Ribosomal Protein L17 (RPL17, Accession NM_000985). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPL17. Src Family Associated Phosphoprotein 2 (SCAP2, Accession NM_003930) is another VGAM134 host target gene. SCAP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAP2 BINDING SITE, designated SEQ ID:10028, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10342] Another function of VGAM134 is therefore inhibition of Src Family Associated Phosphoprotein 2 (SCAP2, Accession NM_003930), a gene which interacts with Src family protein tyrosine kinases and SLAP/FYB (SLA). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAP2. The function of SCAP2 has been established by previous studies. Src family kinases (e.g., FYN; 137025) are involved in signal transduction of tyrosine and nontyrosine kinase receptors in a variety of cells. The Src kinase-associated phosphoprotein SKAP55 (OMIM Ref. No. 604969) is a constitutively tyrosine-phosphorylated, 55-kD protein that interacts with FYN and FYB (OMIM Ref. No. 602731) in T lymphocytes. Marie-Cardine et al. (1998) identified a cDNA encoding SKAP55R, which they called SKAP-HOM (SKAP55 homolog). Western blot and 2-dimensional isoelectric-focusing (IEF)/SDS-PAGE analysis showed that SKAP55R is more basic and migrates more slowly than SKAP55. In contrast to SKAP55, which is preferentially expressed in T cells, Northern blot analysis detected nearly ubiquitous expression of a 4.2-kb SKAP55R transcript as well as testis-specific 1.3- and 2.2-kb transcripts. Immunoblot analysis demonstrated that unlike

SKAP55, SKAP55R is not constitutively phosphorylated in T cells. The authors found that FYN but not LCK (OMIM Ref. No. 153390) or ZAP70 (OMIM Ref. No. 176947) phosphorylates both SKAP55 and SKAP55R.

[10343] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10344] Liu, J.; Kang, H.; Raab, M.; da Silva, A. J.; Kraeft, S.-K.; Rudd, C. E. : FYB (FYN binding protein) serves as a binding partner for lymphoid protein and FYN kinase substrate SKAP55 and a SKAP55-related protein in T cells. *Proc. Nat. Acad. Sci.* 95: 8779–8784, 1998. ; and

[10345] Marie-Cardine, A.; Verhagen, A. M.; Eckerskorn, C.; Schraven, B. : SKAP-HOM, a novel adaptor protein homologous to the FYN-associated protein SKAP55. *FEBS Lett.* 435: 55–60, 1998.

[10346] Further studies establishing the function and utilities of SCAP2 are found in John Hopkins OMIM database record ID 605215, and in cited publications numbered 6966–6968 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 15 Open Reading Frame 5 (C15orf5, Accession NM_030944) is another VGAM134 host target

gene. C15orf5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C15orf5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C15orf5 BINDING SITE, designated SEQ ID:25213, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10347] Another function of VGAM134 is therefore inhibition of Chromosome 15 Open Reading Frame 5 (C15orf5, Accession NM_030944). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C15orf5. FLJ13105 (Accession NM_025001) is another VGAM134 host target gene. FLJ13105 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13105, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13105 BINDING SITE, designated SEQ ID:24571, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ

ID:2845.

[10348] Another function of VGAM134 is therefore inhibition of FLJ13105 (Accession NM_025001). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13105. KIAA1198 (Accession XM_032674) is another VGAM134 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31710, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10349] Another function of VGAM134 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1795 (Accession XM_050988) is another VGAM134 host target gene. KIAA1795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1795, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1795 BINDING SITE, designated SEQ ID:35701, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10350] Another function of VGAM134 is therefore inhibition of KIAA1795 (Accession XM_050988). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1795. KIAA1915 (Accession XM_055481) is another VGAM134 host target gene. KIAA1915 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1915 BINDING SITE, designated SEQ ID:36269, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10351] Another function of VGAM134 is therefore inhibition of KIAA1915 (Accession XM_055481). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1915. LOC158798 (Accession XM_088671) is another VGAM134 host target gene. LOC158798 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158798 BINDING SITE, designated SEQ ID:39892, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10352] Another function of VGAM134 is therefore inhibition of LOC158798 (Accession XM_088671). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158798. LOC221486 (Accession XM_165760) is another VGAM134 host target gene. LOC221486 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221486 BINDING SITE, designated SEQ ID:43744, to

the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10353] Another function of VGAM134 is therefore inhibition of LOC221486 (Accession XM_165760). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221486. LOC51605 (Accession NM_015939) is another VGAM134 host target gene. LOC51605 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51605, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51605 BINDING SITE, designated SEQ ID:18061, to the nucleotide sequence of VGAM134 RNA, herein designated VGAM RNA, also designated SEQ ID:2845.

[10354] Another function of VGAM134 is therefore inhibition of LOC51605 (Accession NM_015939). Accordingly, utilities of VGAM134 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51605. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 135 (VGAM135) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10355] VGAM135 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM135 was detected is described hereinabove with reference to Figs. 1–8.

[10356] VGAM135 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10357] VGAM135 gene encodes a VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM135 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM135 precursor RNA is designated SEQ ID:121, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:121 is located at position 145555 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform

virus).

[10358] VGAM135 precursor RNA folds onto itself, forming VGAM135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10359] An enzyme complex designated DICER COMPLEX, `dices` the VGAM135 folded precursor RNA into VGAM135 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM135 RNA is designated SEQ ID:2846, and is provided hereinbelow with reference to the sequence listing part.

[10360] VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM135 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10361] VGAM135 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM135 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM135 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10362] The complementary binding of VGAM135 RNA, herein designated VGAM RNA, to host target binding sites on VGAM135 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM135 host target RNA into VGAM135 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10363] It is appreciated that VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM135 host target genes. The mRNA of each one of this plurality of VGAM135 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM135 RNA, herein designated VGAM RNA, and which when bound by VGAM135 RNA causes inhibition of translation of respective one or more VGAM135 host target proteins.

[10364] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM135 gene, herein designated VGAM GENE, on one or more VGAM135 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10365] It is yet further appreciated that a function of VGAM135 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific func-

tions, and accordingly utilities, of VGAM135 correlate with, and may be deduced from, the identity of the host target genes which VGAM135 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10366] Nucleotide sequences of the VGAM135 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM135 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM135 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM135 are further described hereinbelow with reference to Table 1.

[10367] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM135 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM135 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10368] As mentioned hereinabove with reference to Fig. 1, a function of VGAM135 gene, herein designated VGAM is inhibition of expression of VGAM135 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM135 correlate with, and may be deduced from, the identity of the target genes which VGAM135 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10369] Adenylate Kinase 3 (AK3, Accession NM_013410) is a VGAM135 host target gene. AK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AK3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AK3 BINDING SITE, designated SEQ ID:15073, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10370] A function of VGAM135 is therefore inhibition of Adenylate Kinase 3 (AK3, Accession NM_013410), a gene which Adenylate kinase 3; strongly similar to murine Ak4. Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AK3. The function of AK3 has been established by previous studies. The adenylate kinases are a family of structurally and functionally related enzymes that catalyze a similar reaction, $\text{MgNTP} + \text{AMP} = \text{MgNDP} +$

ADP (N = A or G). The AK enzymes are important for maintenance of homeostasis of the adenine and guanine nucleotide pools. AK1 (OMIM Ref. No. 103000) is a cytosolic enzyme for which ATP is the substrate. AK2 (OMIM Ref. No. 103020) catalyzes the same reaction as AK1, but it is localized in the mitochondrial intermembrane space. AK3 is present in the mitochondrial matrix and prefers GTP over ATP as the substrate. Wilson et al. (1976) pointed out that AK3 is nucleosidetriphosphate-adenylate kinase. In the course of their efforts to identify the gene causing neurofibromatosis (NF1; 162200), Viskochil et al. (1990) found a gene first designated HB15, which Xu et al. (1992) subsequently concluded is probably a processed pseudogene of AK3. It is intronless and contains a polyadenylate tract, but retains coding potential because the open reading frame was not impaired by any observed base substitutions. One presumed processed pseudogene of AK3 is located within an intron of the NF1 gene. Xu et al. (1992) also characterized cDNA clones for the authentic AK3. By study of somatic cell hybrids, Povey et al. (1976) assigned AK3 to chromosome 9. The SRO (smallest region of overlap) for AK3 was estimated to be 9p24-p13 (Robson and Meera Khan, 1982). By interspecific back-

cross linkage analysis, Pilz et al. (1995) mapped the Ak3 gene to mouse chromosome 4. Gene map locus 9p24–p13

[10371] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10372] Xu, G.; O'Connell, P.; Stevens, J.; White, R. : Characterization of human adenylate kinase 3 (AK3) cDNA and mapping of the AK3 pseudogene to an intron of the NF1 gene. Genomics 13: 537–542, 1992. ; and

[10373] Pilz, A.; Woodward, K.; Povey, S.; Abbott, C. : Comparative mapping of 50 human chromosome 9 loci in the laboratory mouse. Genomics 25: 139–149, 1995.

[10374] Further studies establishing the function and utilities of AK3 are found in John Hopkins OMIM database record ID 103030, and in cited publications numbered 802–810 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ11210 (Accession XM_005298) is another VGAM135 host target gene. FLJ11210 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu–

cleotide sequences of FLJ11210 BINDING SITE, designated SEQ ID:29975, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10375] Another function of VGAM135 is therefore inhibition of FLJ11210 (Accession XM_005298). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11210. KIAA1145 (Accession XM_037790) is another VGAM135 host target gene. KIAA1145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1145 BINDING SITE, designated SEQ ID:32682, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10376] Another function of VGAM135 is therefore inhibition of KIAA1145 (Accession XM_037790). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1145. MGC13105 (Accession XM_049394) is another

VGAM135 host target gene. MGC13105 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13105, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13105 BINDING SITE, designated SEQ ID:35408, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10377] Another function of VGAM135 is therefore inhibition of MGC13105 (Accession XM_049394). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13105. LOC200014 (Accession XM_114087) is another VGAM135 host target gene. LOC200014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42690, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10378] Another function of VGAM135 is therefore inhibition of LOC200014 (Accession XM_114087). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. LOC202934 (Accession XM_117486) is another VGAM135 host target gene. LOC202934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202934 BINDING SITE, designated SEQ ID:43467, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10379] Another function of VGAM135 is therefore inhibition of LOC202934 (Accession XM_117486). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202934. LOC255465 (Accession XM_173206) is another VGAM135 host target gene. LOC255465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255465, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255465 BINDING SITE, designated SEQ ID:46459, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10380] Another function of VGAM135 is therefore inhibition of LOC255465 (Accession XM_173206). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255465. LOC257319 (Accession XM_171049) is another VGAM135 host target gene. LOC257319 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257319, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257319 BINDING SITE, designated SEQ ID:45835, to the nucleotide sequence of VGAM135 RNA, herein designated VGAM RNA, also designated SEQ ID:2846.

[10381] Another function of VGAM135 is therefore inhibition of LOC257319 (Accession XM_171049). Accordingly, utilities of VGAM135 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC257319. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 136 (VGAM136) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10382] VGAM136 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM136 was detected is described hereinabove with reference to Figs. 1–8.

[10383] VGAM136 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10384] VGAM136 gene encodes a VGAM136 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM136 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM136 precursor RNA is designated SEQ ID:122, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:122 is located at position 91976 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10385] VGAM136 precursor RNA folds onto itself, forming VGAM136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10386] An enzyme complex designated DICER COMPLEX, `dices` the VGAM136 folded precursor RNA into VGAM136 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM136 RNA is designated SEQ ID:2847, and is provided hereinbelow with reference to the sequence

listing part.

[10387] VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM136 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10388] VGAM136 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM136 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM136 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10389] The complementary binding of VGAM136 RNA, herein designated VGAM RNA, to host target binding sites on VGAM136 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM136 host target RNA into VGAM136 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10390] It is appreciated that VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM136 host target genes. The mRNA of each one of this plurality of VGAM136 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM136 RNA, herein designated VGAM

RNA, and which when bound by VGAM136 RNA causes inhibition of translation of respective one or more VGAM136 host target proteins.

[10391] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM136 gene, herein designated VGAM GENE, on one or more VGAM136 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10392] It is yet further appreciated that a function of VGAM136 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM136 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM136 correlate with, and may be deduced from, the identity of the host target genes which VGAM136 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10393] Nucleotide sequences of the VGAM136 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM136 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM136 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM136 are further described hereinbelow with reference to Table 1.

[10394] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM136 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM136 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10395] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM136 gene, herein designated VGAM is inhibition of expression of VGAM136 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM136 correlate with, and may be deduced from, the identity of the target genes which VGAM136 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10396] Jagged 2 (JAG2, Accession NM_002226) is a VGAM136 host target gene. JAG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAG2 BINDING SITE, designated SEQ ID:8006, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10397] A function of VGAM136 is therefore inhibition of Jagged 2 (JAG2, Accession NM_002226), a gene which is a putative notch ligand involved in the mediation of notch signaling. Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAG2. The function of JAG2 has been es-

established by previous studies. The Notch signaling pathway is a conserved intercellular signaling mechanism that is essential for proper embryonic development in numerous metazoan organisms. Members of the Notch gene family (see OMIM Ref. No. NOTCH1; 190198) encode transmembrane receptors that are critical for various cell fate decisions. Multiple ligands that activate Notch and related receptors have been identified, including Serrate and Delta in *Drosophila* and JAG1 (OMIM Ref. No. 601920) in vertebrates. By searching for human brain expressed sequence tags (ESTs) homologous to Serrate and Delta, Luo et al. (1997) identified a cDNA which they called Jagged-2 (JAG2). The predicted 1,238-amino acid JAG2 protein has several recognizable motifs, including a signal peptide, 16 EGF-like repeats, a transmembrane domain, and a short cytoplasmic domain. The amino acid sequence of human JAG2 is 89% identical to that of rat Jag2. Northern blot analysis and in situ hybridization showed expression of Jag2 in various murine tissues. Immunohistochemistry revealed coexpression of Jag2 and Notch1 within murine fetal thymus and other murine fetal tissues. Coculture of fibroblasts expressing human JAG2 with murine C2C12 myoblasts inhibited myogenic differentiation. This effect

was simulated by expression of constitutively active Notch1, suggesting that JAG2 engages the Notch1 pathway of signal transduction. Gray et al. (1999) also cloned JAG2, which they called HJ2. Northern blot analysis revealed expression of a 5.3-kb JAG2 transcript in heart and skeletal muscle, with weaker expression in pancreas. In situ hybridization analysis indicated upregulated expression of JAG2 in squamous cell carcinoma. Animal model experiments lend further support to the function of JAG2. Jiang et al. (1998) examined the in vivo role of the Jag2 gene by making a targeted mutation that removed a domain of the Jagged-2 protein required for receptor interaction. Mice homozygous for this deletion died perinatally because of defects in craniofacial morphogenesis. The mutant homozygotes exhibited cleft palate and fusion of the tongue with the palatal shelves. They also exhibited syndactyly of the fore- and hindlimbs. The apical ectodermal ridge (AER) of the limb buds of the mutant homozygotes was hyperplastic, and Jiang et al. (1998) observed an expanded domain of Fgf8 (OMIM Ref. No. 600483) expression in the AER. In the foot plates of the mutant homozygotes, both Bmp2 (OMIM Ref. No. 112261) and Bmp7 (OMIM Ref. No. 112267) expression and apoptotic inter-

digital cell death were reduced. Mutant homozygotes also displayed defects in thymic development, exhibiting altered thymic morphology and impaired differentiation of T cells of the gamma/delta lineage. These results demonstrated that Notch signaling mediated by Jag2 plays an essential role during limb, craniofacial, and thymic development in mice.

[10398] It is appreciated that the abovementioned animal model for JAG2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10399] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10400] Lanford, P. J.; Lan, Y.; Jiang, R.; Lindsell, C.; Weinmaster, G.; Gridley, T.; Kelley, M. W. : Notch signalling pathway mediates hair cell development in mammalian cochlea. Nature Genet. 21: 289–292, 1999. ; and

[10401] Gray, G. E.; Mann, R. S.; Mitsiadis, E.; Henrique, D.; Carcangiu, M.–L.; Banks, A.; Leiman, J.; Ward, D.; Ish-Horowitz, D.; Artavanis–Tsakonas, S. : Human ligands of the Notch receptor.

[10402] Further studies establishing the function and utilities of

JAG2 are found in John Hopkins OMIM database record ID 602570, and in cited publications numbered 126 and 6218–6221 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Synaptobrevin-like 1 (SYBL1, Accession NM_005638) is another VGAM136 host target gene. SYBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYBL1 BINDING SITE, designated SEQ ID:12166, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10403] Another function of VGAM136 is therefore inhibition of Synaptobrevin-like 1 (SYBL1, Accession NM_005638), a gene which is synaptobrevin-like 1 and is similar to synaptobrevin. Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYBL1. The function of SYBL1 has been established by previous studies. From a search for expressed genes in the Xq28 pseudoautosomal region (PAR), D'Esposito et al. (1996) described a

2,576-bp cDNA encoding a synaptobrevin-like gene. The gene, tentatively named SYBL1 by them, encodes a 220-amino acid polypeptide of 25 kD with 60% similarity (37.5% homology) to an unpublished Arabidopsis gene sequence. SYBL1 was found, unlike all Xp pseudoautosomal genes studied to that time, to undergo X inactivation. In addition, it is also inactive on the Y chromosome, thereby maintaining dosage compensation in an unprecedented way. (The synaptobrevin genes, SYB1 (OMIM Ref. No. 185880) and SYB2 (OMIM Ref. No. 185881), are autosomal, being located on chromosomes 12 and 17, respectively.) In studies of the pseudoautosomal regions of the X and Y chromosomes, Ciccodicola et al. (2000) sequenced the telomeric 400 kb of the long arm of the human X chromosome, including 330 kb of the human Xq/Yq pseudoautosomal region and the telomere. Sequencing revealed subregions with distinctive regulatory and evolutionary features. The proximal 295 kb contains 2 genes inactivated on both the inactive X and Y chromosomes: SYBL1 and a human homolog of 'sprouty' in Drosophila. The GC-rich distal 35 kb, added in stages and much later in evolution, contains the X/Y expressed gene IL9R (OMIM Ref. No. 300007) and the gene CXYorf1 only 5 kb from

the Xq telomere. These properties make Xq/YqPAR a model for studies of region-specific gene inactivation, telomere evolution, and involvement in sex-limited conditions.

[10404] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10405] Ciccodicola, A.; D'Esposito, M.; Esposito, T.; Gianfrancesco, F.; Migliaccio, C.; Miano, M. G.; Matarazzo, M. R.; Vacca, M.; Franze, A.; Cuccurese, M.; Cocchia, M.; Curci, A. : Differentially regulated and evolved genes in the fully sequenced Xq/Yq pseudoautosomal region. Hum. Molec. Genet. 9: 395-401, 2000. ; and

[10406] D'Esposito, M.; Ciccodicola, A.; Gianfrancesco, F.; Esposito, T.; Flagiello, L.; Mazzearella, R.; Schlessinger, D.; D'Urso, M. : A synaptobrevin-like gene in the Xq28 pseudoautosomal re.

[10407] Further studies establishing the function and utilities of SYBL1 are found in John Hopkins OMIM database record ID 300053, and in cited publications numbered 9001-9004 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ10900 (Accession XM_037744) is another VGAM136 host target

gene. FLJ10900 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ10900, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10900 BINDING SITE, designated SEQ ID:32669, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10408] Another function of VGAM136 is therefore inhibition of FLJ10900 (Accession XM_037744). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10900. FLJ20294 (Accession NM_017749) is another VGAM136 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294 BINDING SITE, designated SEQ ID:19347, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10409] Another function of VGAM136 is therefore inhibition of FLJ20294 (Accession NM_017749). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20294. FLJ20297 (Accession NM_017951) is another VGAM136 host target gene. FLJ20297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20297 BINDING SITE, designated SEQ ID:19647, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10410] Another function of VGAM136 is therefore inhibition of FLJ22690 (Accession NM_024711). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22690. FLJ22690 (Accession NM_024711) is another VGAM136 host target gene. FLJ22690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22690 BINDING SITE, designated SEQ ID:24037, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10411] Another function of VGAM136 is therefore inhibition of FLJ22690 (Accession NM_024711). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22690. JM11 (Accession NM_033626) is another VGAM136 host target gene. JM11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JM11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JM11 BINDING SITE, designated SEQ ID:27327, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10412] Another function of VGAM136 is therefore inhibition of JM11 (Accession NM_033626). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JM11.

Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186) is another VGAM136 host target gene. KCNB2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNB2 BINDING SITE, designated SEQ ID:45964, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10413] Another function of VGAM136 is therefore inhibition of Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNB2. KIAA0064 (Accession NM_014748) is another VGAM136 host target gene. KIAA0064 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0064 BINDING SITE, designated SEQ ID:16459, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10414] Another function of VGAM136 is therefore inhibition of KIAA0064 (Accession NM_014748). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0064. KIAA0202 (Accession XM_034872) is another VGAM136 host target gene. KIAA0202 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0202, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0202 BINDING SITE, designated SEQ ID:32179, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10415] Another function of VGAM136 is therefore inhibition of KIAA0202 (Accession XM_034872). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0202. KIAA0237 (Accession NM_014747) is another VGAM136 host target gene. KIAA0237 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16438, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10416] Another function of VGAM136 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0682 (Accession NM_014852) is another VGAM136 host target gene. KIAA0682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0682 BINDING SITE, designated SEQ ID:16900, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10417] Another function of VGAM136 is therefore inhibition of

KIAA0682 (Accession NM_014852). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0682. KIAA1297 (Accession XM_051005) is another VGAM136 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35708, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10418] Another function of VGAM136 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. PB1 (Accession NM_018313) is another VGAM136 host target gene. PB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PB1 BINDING SITE, designated SEQ ID:20307, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10419] Another function of VGAM136 is therefore inhibition of PB1 (Accession NM_018313). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PB1. POLD3 (Accession XM_166243) is another VGAM136 host target gene. POLD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLD3 BINDING SITE, designated SEQ ID:44055, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10420] Another function of VGAM136 is therefore inhibition of POLD3 (Accession XM_166243). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLD3. ZER6 (Accession XM_032742) is another VGAM136 host

target gene. ZER6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZER6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZER6 BINDING SITE, designated SEQ ID:31742, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10421] Another function of VGAM136 is therefore inhibition of ZER6 (Accession XM_032742). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZER6. LOC146485 (Accession XM_007966) is another VGAM136 host target gene. LOC146485 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146485 BINDING SITE, designated SEQ ID:30071, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10422] Another function of VGAM136 is therefore inhibition of LOC146485 (Accession XM_007966). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146485. LOC153443 (Accession XM_087669) is another VGAM136 host target gene. LOC153443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153443 BINDING SITE, designated SEQ ID:39372, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10423] Another function of VGAM136 is therefore inhibition of LOC153443 (Accession XM_087669). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153443. LOC153910 (Accession XM_087801) is another VGAM136 host target gene. LOC153910 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153910, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153910 BINDING SITE, designated SEQ ID:39439, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10424] Another function of VGAM136 is therefore inhibition of LOC153910 (Accession XM_087801). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153910. LOC221421 (Accession XM_166428) is another VGAM136 host target gene. LOC221421 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221421, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221421 BINDING SITE, designated SEQ ID:44320, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10425] Another function of VGAM136 is therefore inhibition of LOC221421 (Accession XM_166428). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221421. LOC253805 (Accession XM_172854) is another VGAM136 host target gene. LOC253805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253805 BINDING SITE, designated SEQ ID:46131, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10426] Another function of VGAM136 is therefore inhibition of LOC253805 (Accession XM_172854). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253805. LOC90190 (Accession XM_029758) is another VGAM136 host target gene. LOC90190 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90190, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90190 BINDING SITE, designated SEQ ID:30946, to the nucleotide sequence of VGAM136 RNA, herein designated

VGAM RNA, also designated SEQ ID:2847.

[10427] Another function of VGAM136 is therefore inhibition of LOC90190 (Accession XM_029758). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90190. LOC91115 (Accession XM_036218) is another VGAM136 host target gene. LOC91115 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91115, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91115 BINDING SITE, designated SEQ ID:32399, to the nucleotide sequence of VGAM136 RNA, herein designated VGAM RNA, also designated SEQ ID:2847.

[10428] Another function of VGAM136 is therefore inhibition of LOC91115 (Accession XM_036218). Accordingly, utilities of VGAM136 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91115. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 137 (VGAM137) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10429] VGAM137 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM137 was detected is described hereinabove with reference to Figs. 1–8.

[10430] VGAM137 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10431] VGAM137 gene encodes a VGAM137 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM137 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM137 precursor RNA is designated SEQ ID:123, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:123 is located at position 74213 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10432] VGAM137 precursor RNA folds onto itself, forming VGAM137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10433] An enzyme complex designated DICER COMPLEX, `dices` the VGAM137 folded precursor RNA into VGAM137 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM137 RNA is designated SEQ ID:2848, and is provided hereinbelow with reference to the sequence listing part.

[10434] VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM137 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM137 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10435] VGAM137 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM137 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM137 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10436] The complementary binding of VGAM137 RNA, herein designated VGAM RNA, to host target binding sites on VGAM137 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM137 host target RNA into VGAM137 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10437] It is appreciated that VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM137 host target genes. The mRNA of each one of this plurality of VGAM137 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM137 RNA, herein designated VGAM RNA, and which when bound by VGAM137 RNA causes inhibition of translation of respective one or more VGAM137 host target proteins.

[10438] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM137 gene, herein designated VGAM GENE, on one or more VGAM137 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10439] It is yet further appreciated that a function of VGAM137 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM137 correlate

with, and may be deduced from, the identity of the host target genes which VGAM137 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10440] Nucleotide sequences of the VGAM137 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM137 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM137 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM137 are further described hereinbelow with reference to Table 1.

[10441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM137 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM137 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10442] As mentioned hereinabove with reference to Fig. 1, a function of VGAM137 gene, herein designated VGAM is inhibition of expression of VGAM137 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM137 correlate with, and may be deduced

from, the identity of the target genes which VGAM137 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10443] Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476) is a VGAM137 host target gene. BTN2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A1 BINDING SITE, designated SEQ ID:27801, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10444] A function of VGAM137 is therefore inhibition of Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A1. Cat Eye Syndrome Chromosome Region, Candidate 6 (CECR6, Accession NM_031890) is another VGAM137 host target gene. CECR6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CECR6,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CECR6 BINDING SITE, designated SEQ ID:25636, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10445] Another function of VGAM137 is therefore inhibition of Cat Eye Syndrome Chromosome Region, Candidate 6 (CECR6, Accession NM_031890). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CECR6. Enabled Homolog (Drosophila) (ENAH, Accession NM_018212) is another VGAM137 host target gene. ENAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAH BINDING SITE, designated SEQ ID:20125, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10446] Another function of VGAM137 is therefore inhibition of

Enabled Homolog (Drosophila) (ENAH, Accession NM_018212). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAH. FLJ11110 (Accession NM_018326) is another VGAM137 host target gene. FLJ11110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11110 BINDING SITE, designated SEQ ID:20320, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10447] Another function of VGAM137 is therefore inhibition of FLJ11110 (Accession NM_018326). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11110. KIAA0884 (Accession XM_046660) is another VGAM137 host target gene. KIAA0884 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0884 BINDING SITE, designated SEQ ID:34775, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10448] Another function of VGAM137 is therefore inhibition of KIAA0884 (Accession XM_046660). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0884. LOC163682 (Accession XM_099402) is another VGAM137 host target gene. LOC163682 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC163682, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163682 BINDING SITE, designated SEQ ID:42085, to the nucleotide sequence of VGAM137 RNA, herein designated VGAM RNA, also designated SEQ ID:2848.

[10449] Another function of VGAM137 is therefore inhibition of LOC163682 (Accession XM_099402). Accordingly, utilities of VGAM137 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC163682. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 138 (VGAM138) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10450] VGAM138 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM138 was detected is described hereinabove with reference to Figs. 1–8.

[10451] VGAM138 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10452] VGAM138 gene encodes a VGAM138 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM138 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM138 precursor RNA is designated SEQ ID:124, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:124 is located at position 4877 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10453] VGAM138 precursor RNA folds onto itself, forming VGAM138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10454] An enzyme complex designated DICER COMPLEX, `dices` the VGAM138 folded precursor RNA into VGAM138 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM138 RNA is designated SEQ ID:2849, and is provided hereinbelow with reference to the sequence listing part.

[10455] VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM138 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10456] VGAM138 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM138 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM138 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10457] The complementary binding of VGAM138 RNA, herein designated VGAM RNA, to host target binding sites on VGAM138 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM138 host target RNA into VGAM138 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10458] It is appreciated that VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM138 host target genes. The mRNA of each one of this plurality of VGAM138 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM138 RNA, herein designated VGAM RNA, and which when bound by VGAM138 RNA causes in-

hibition of translation of respective one or more VGAM138 host target proteins.

[10459] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM138 gene, herein designated VGAM GENE, on one or more VGAM138 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10460] It is yet further appreciated that a function of VGAM138 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM138 include diagnosis, prevention and

treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM138 correlate with, and may be deduced from, the identity of the host target genes which VGAM138 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10461] Nucleotide sequences of the VGAM138 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM138 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM138 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM138 are further described hereinbelow with reference to Table 1.

[10462] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM138 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM138 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10463] As mentioned hereinabove with reference to Fig. 1, a function of VGAM138 gene, herein designated VGAM is

inhibition of expression of VGAM138 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM138 correlate with, and may be deduced from, the identity of the target genes which VGAM138 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10464] Pallidin Homolog (mouse) (PLDN, Accession NM_012388) is a VGAM138 host target gene. PLDN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PLDN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLDN BINDING SITE, designated SEQ ID:14744, to the nucleotide sequence of VGAM138 RNA, herein designated VGAM RNA, also designated SEQ ID:2849.

[10465] A function of VGAM138 is therefore inhibition of Pallidin Homolog (mouse) (PLDN, Accession NM_012388), a gene which may play a role in intracellular vesicle trafficking. Accordingly, utilities of VGAM138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLDN. The function of PLDN has been established by previous studies. 'Pallid' is 1 of 13 platelet

storage pool deficiency (SPD) mouse mutants. Pallid (pa) animals suffer from prolonged bleeding time, pigment dilution, kidney lysosomal enzyme elevation, serum alpha-1-antitrypsin (OMIM Ref. No. 107400) activity deficiency, and abnormal otolith formation. As with other mouse mutants of this class, characterization of pallid mice suggested a defect in organelle biosynthesis. Huang et al. (1999) described the physical mapping, positional cloning, and mutational and functional analysis of the gene that is defective in pallid mice. The gene encodes a ubiquitously expressed, highly charged 172-amino acid protein, which they called pallidin, with no homology to known proteins. Huang et al. (1999) detected a nonsense mutation at codon 69 of this gene in the pallid mutant. Using a yeast 2-hybrid screen, Huang et al. (1999) discovered that pallidin interacts with syntaxin-13, a t-SNARE protein that mediates vesicle docking and fusion. Huang et al. (1999) confirmed this interaction by coimmunoprecipitation assay. Immunofluorescence studies corroborated that the cellular distribution of pallidin overlaps that of syntaxin-13. Whereas the 'mocha' (OMIM Ref. No. 607246) and 'pearl' (OMIM Ref. No. 603401) SPD mutants have defects in Ap3, the findings of Huang et al. (1999) suggested that

pallid SPD mutants are defective in a more downstream event of vesicle trafficking, namely vesicle docking and fusion. Huang et al. (1999) stated that 'pallid' was the fifth storage pool deficiency mutant to be described at the molecular level. These mutants are characterized by abnormalities in platelet-dense granules, melanosomes, and lysosomes, and in each case, the predicted protein is involved in organelle biogenesis. Huang et al. (1999) isolated the orthologous gene encoding human pallidin and found that the predicted protein has 86% amino acid identity with the mouse protein. The human pallidin cDNA sequence has been deposited in GenBank (AF080470). By coimmunoprecipitation and immunodepletion experiments of mouse skin fibroblasts, Falcon-Perez et al. (2002) identified pallidin as a component of BLOC1 (biogenesis of lysosome-related organelles complex-1), which also contains muted (OMIM Ref. No. 607289). A yeast 2-hybrid screen found no direct interaction between muted and pallidin, but pallidin was found to interact with itself. Residues that include 2 putative coiled-coil domains of human palladin were necessary and sufficient for self-assembly. Falcon-Perez et al. (2002) also determined that pallidin/BLOC1 could interact with actin filaments in vitro

and in transfected cells. Huang (2000) stated that ESTs of the human PA gene had been mapped to 15q15 by radiation hybrid mapping. By ancestral chromosome mapping, Huang et al. (1999) localized the mouse pallidin gene to chromosome 2E. The pallidin gene is closely linked to mouse Epb42 (OMIM Ref. No. 171070) and B2m (OMIM Ref. No. 109700), 68 cM from the centromere.

[10466] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10467] Falcon-Perez, J. M.; Starcevic, M.; Gautam, R.; Dell'Angelica, E. C. : BLOC-1, a novel complex containing the pallidin and muted proteins involved in the biogenesis of melanosomes and platelet-dense granules. J. Biol. Chem. 277: 28191-28199, 2002. ; and

[10468] Huang, L.; Kuo, Y.-M.; Gitschier, J. : The pallid gene encodes a novel, syntaxin 13-interacting protein involved in platelet storage pool deficiency. Nature Genet. 23: 329-332, 1999.

[10469] Further studies establishing the function and utilities of PLDN are found in John Hopkins OMIM database record ID 604310, and in cited publications numbered 7439-7441 listed in the bibliography section hereinbelow, which are

also hereby incorporated by reference. MGC3101 (Accession NM_024043) is another VGAM138 host target gene. MGC3101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3101 BINDING SITE, designated SEQ ID:23477, to the nucleotide sequence of VGAM138 RNA, herein designated VGAM RNA, also designated SEQ ID:2849.

[10470] Another function of VGAM138 is therefore inhibition of MGC3101 (Accession NM_024043). Accordingly, utilities of VGAM138 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3101. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 139 (VGAM139) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10471] VGAM139 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM139 was detected is described hereinabove with reference to Figs. 1–8.

[10472] VGAM139 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10473] VGAM139 gene encodes a VGAM139 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM139 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM139 precursor RNA is designated SEQ ID:125, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:125 is located at position 193809 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10474] VGAM139 precursor RNA folds onto itself, forming VGAM139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10475] An enzyme complex designated DICER COMPLEX, `dices` the VGAM139 folded precursor RNA into VGAM139 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM139 RNA is designated SEQ ID:2850, and is provided hereinbelow with reference to the sequence listing part.

[10476] VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM139 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[10477] VGAM139 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM139 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM139 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10478] The complementary binding of VGAM139 RNA, herein designated VGAM RNA, to host target binding sites on VGAM139 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM139 host target RNA into VGAM139 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10479] It is appreciated that VGAM139 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM139 host target genes. The mRNA of each one of this plurality of VGAM139 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM139 RNA, herein designated VGAM RNA, and which when bound by VGAM139 RNA causes inhibition of translation of respective one or more VGAM139 host target proteins.

[10480] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM139 gene, herein designated VGAM GENE, on one or more VGAM139 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10481] It is yet further appreciated that a function of VGAM139 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM139 correlate with, and may be deduced from, the identity of the host target genes which VGAM139 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [10482] Nucleotide sequences of the VGAM139 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM139 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM139 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM139 are further described hereinbelow with reference to Table 1.
- [10483] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM139 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM139 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [10484] As mentioned hereinabove with reference to Fig. 1, a function of VGAM139 gene, herein designated VGAM is inhibition of expression of VGAM139 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM139 correlate with, and may be deduced from, the identity of the target genes which VGAM139 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [10485] Nuclear Receptor Subfamily 4, Group A, Member 2

(NR4A2, Accession NM_006186) is a VGAM139 host target gene. NR4A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR4A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR4A2 BINDING SITE, designated SEQ ID:12855, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10486] A function of VGAM139 is therefore inhibition of Nuclear Receptor Subfamily 4, Group A, Member 2 (NR4A2, Accession NM_006186), a gene which may be a general coactivator of transcription. Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR4A2. The function of NR4A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM127. Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFB3, Accession NM_003243) is another VGAM139 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by TGFBR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFBR3 BINDING SITE, designated SEQ ID:9248, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10487] Another function of VGAM139 is therefore inhibition of Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFBR3, Accession NM_003243), a gene which involves in capturing and retaining TGF-beta for presentation to the signaling receptors. Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR3. The function of TGFBR3 has been established by previous studies. In addition to type I TGF-beta receptor (TGFBR1; 190181) and type II (TGFBR2; 190182), type III (OMIM Ref. No. TGFBR3) has been identified. It is a glycoprotein that binds TGF-beta and exists in both a membrane-bound and a soluble form. It may serve as a receptor accessory molecule in both the TGF-beta and fibroblast growth factor systems. TGFBR3 lacks a recognizable signaling domain and has no clearly defined role in TGF-beta signal-

ing. To investigate TGFBR3 function, Brown et al. (1999) studied cardiac endothelial cells in chick atrioventricular cushion explants. Endothelial cells undergoing epithelial-mesenchymal transformation expressed TGFBR3, and TGFBR3-specific antisera were found to inhibit mesenchyme formation and migration. Misexpression of TGFBR3 in nontransforming ventricular endothelial cells conferred transformation in response to TGF β 2. These results supported a model where TGFBR3 localizes transformation in the heart and plays an essential, nonredundant role in TGF β -signaling. Lewis et al. (2000) demonstrated that the type III TGF β -receptor, or beta-glycan, can function as an inhibin (see OMIM Ref. No. 147380) coreceptor with ActRII (OMIM Ref. No. 102581). Beta-glycan binds inhibin with high affinity and enhances binding in cells coexpressing ActRII and beta-glycan. Inhibin also forms crosslinked complexes with both recombinant and endogenously expressed beta-glycan and ActRII. Lewis et al. (2000) demonstrated that beta-glycan confers inhibin sensitivity to cell lines that otherwise respond poorly to this hormone. The ability of beta-glycan to inhibit to facilitate inhibin antagonism of activin (see OMIM Ref. No. 147290) provided a variation on the emerging

roles of proteoglycans as coreceptors modulating ligand-receptor sensitivity, selectivity, and function.

[10488] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10489] Brown, C. B.; Boyer, A. S.; Runyan, R. B.; Barnett, J. V. : Requirement of type III TGF-beta receptor for endocardial cell transformation in the heart. Science 283: 2080-2082, 1999. ; and

[10490] Lewis, K. A.; Gray, P. C.; Blount, A. L.; MacConell, L. A.; Wiater, E.; Bilezikjian, L. M.; Vale, W. : Betaglycan binds inhibin and can mediate functional antagonism of activin signalling.

[10491] Further studies establishing the function and utilities of TGFBR3 are found in John Hopkins OMIM database record ID 600742, and in cited publications numbered 757 and 7580 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ10560 (Accession NM_018138) is another VGAM139 host target gene. FLJ10560 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10560, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10560 BINDING SITE, designated SEQ ID:19936, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10492] Another function of VGAM139 is therefore inhibition of FLJ10560 (Accession NM_018138). Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10560. FLJ20727 (Accession NM_017944) is another VGAM139 host target gene. FLJ20727 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20727 BINDING SITE, designated SEQ ID:19638, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10493] Another function of VGAM139 is therefore inhibition of FLJ20727 (Accession NM_017944). Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20727.

KIAA1775 (Accession NM_033100) is another VGAM139 host target gene. KIAA1775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1775 BINDING SITE, designated SEQ ID:26943, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10494] Another function of VGAM139 is therefore inhibition of KIAA1775 (Accession NM_033100). Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1775. Synaptopodin 2 (SYNPO2, Accession XM_050219) is another VGAM139 host target gene. SYNPO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNPO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNPO2 BINDING SITE, designated SEQ ID:35591, to the nucleotide sequence of VGAM139 RNA,

herein designated VGAM RNA, also designated SEQ ID:2850.

[10495] Another function of VGAM139 is therefore inhibition of Synaptopodin 2 (SYNPO2, Accession XM_050219). Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNPO2. TXI1 (Accession NM_018430) is another VGAM139 host target gene. TXI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TXI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TXI1 BINDING SITE, designated SEQ ID:20492, to the nucleotide sequence of VGAM139 RNA, herein designated VGAM RNA, also designated SEQ ID:2850.

[10496] Another function of VGAM139 is therefore inhibition of TXI1 (Accession NM_018430). Accordingly, utilities of VGAM139 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TXI1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger

140 (VGAM140) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10497] VGAM140 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM140 was detected is described hereinabove with reference to Figs. 1–8.

[10498] VGAM140 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10499] VGAM140 gene encodes a VGAM140 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM140 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM140 precursor RNA is designated SEQ ID:126, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:126 is located at position 51736 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10500] VGAM140 precursor RNA folds onto itself, forming VGAM140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10501] An enzyme complex designated DICER COMPLEX, `dices` the VGAM140 folded precursor RNA into VGAM140 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM140 RNA is designated SEQ ID:2851, and is provided hereinbelow with reference to the sequence listing part.

[10502] VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM140 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM140 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10503] VGAM140 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM140 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM140 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10504] The complementary binding of VGAM140 RNA, herein designated VGAM RNA, to host target binding sites on VGAM140 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM140 host target RNA into VGAM140 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10505] It is appreciated that VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM140 host target genes. The mRNA of each one of this plurality of VGAM140 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM140 RNA, herein designated VGAM RNA, and which when bound by VGAM140 RNA causes inhibition of translation of respective one or more VGAM140 host target proteins.

[10506] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM140 gene, herein designated VGAM GENE, on one or more VGAM140 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10507] It is yet further appreciated that a function of VGAM140 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM140 correlate

with, and may be deduced from, the identity of the host target genes which VGAM140 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10508] Nucleotide sequences of the VGAM140 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM140 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM140 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM140 are further described hereinbelow with reference to Table 1.

[10509] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM140 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM140 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10510] As mentioned hereinabove with reference to Fig. 1, a function of VGAM140 gene, herein designated VGAM is inhibition of expression of VGAM140 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM140 correlate with, and may be deduced

from, the identity of the target genes which VGAM140 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10511] Cullin 4B (CUL4B, Accession NM_003588) is a VGAM140 host target gene. CUL4B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUL4B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUL4B BINDING SITE, designated SEQ ID:9640, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10512] A function of VGAM140 is therefore inhibition of Cullin 4B (CUL4B, Accession NM_003588), a gene which is a negative regulator of the cell cycle in *C. elegans*. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CUL4B. The function of CUL4B has been established by previous studies. Kipreos et al. (1996) identified the cullin gene family, which includes at least 5 members in nematodes, 6 in humans, and 3 in *S. cerevisiae*. See CUL1 (OMIM Ref. No. 603134). Human CUL4A (OMIM Ref. No.

603137) and CUL4B are orthologs of nematode cul4. The partial C-terminal amino acid sequences of CUL4A and CUL4B share 88% identity. Rasooly (1998) found that a brain cDNA isolated by Ishikawa et al. (1998), KIAA0695, was 99% identical to CUL4B. The predicted KIAA0695 protein is 717 amino acids long. Using RT-PCR, Ishikawa et al. (1998) determined that KIAA0695 is expressed ubiquitously. Although Ishikawa et al. (1998) mapped the KIAA0695 gene to human chromosome 10, Rasooly (1998) noted the presence of sequences in GenBank (AC002476) identical to CUL4B within a cloned region in Xq23.

[10513] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10514] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 5: 169–176, 1998. ; and

[10515] Kipreos, E. T.; Lander, L. E.; Wing, J. P.; He, W. W.; Hedgecock, E. M. : cul-1 is required for cell cycle exit in C. ele-

gans and identifies a novel gene family. Cell 85: 829–839, 1996.

[10516] Further studies establishing the function and utilities of CUL4B are found in John Hopkins OMIM database record ID 300304, and in cited publications numbered 9440–9442 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Coagulation Factor II (thrombin) Receptor (F2R, Accession NM_001992) is another VGAM140 host target gene. F2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2R BINDING SITE, designated SEQ ID:7720, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10517] Another function of VGAM140 is therefore inhibition of Coagulation Factor II (thrombin) Receptor (F2R, Accession NM_001992), a gene which Thrombin receptor; G protein-coupled receptor involved in platelet activation. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with F2R. The function of F2R has been established by previous studies. Coughlin et al. (1992) reviewed the cloning and characterization of a platelet thrombin (OMIM Ref. No. 176930) receptor (Vu et al., 1991). The thrombin receptor is structurally related to other members of the 7-transmembrane receptor family and has been isolated from diverse cell types. It is intimately involved in the regulation of the thrombotic response. Using PCR analyses of a human/rodent hybrid cell mapping panel, Bahou et al. (1993) assigned the TR gene to chromosome 5. By fluorescence in situ hybridization, they refined the localization to 5q13, confirming its presence as a single locus in the human genome. Poirier et al. (1996) mapped the Cf2r gene to mouse chromosome 13 by studies of an interspecific backcross. Utilizing 2 distinct radiation hybrid mapping panels with different levels of resolution, Schmidt et al. (1997) demonstrated that this gene, sometimes referred to as PAR1, and the proteinase activated receptor-2 gene (OMIM Ref. No. 600933) are tightly linked. Physical mapping using yeast artificial chromosomes and inversion field gel electrophoresis demonstrated that they are maximally separated by 90 kb. Riewald et al. (2002) demonstrated that activated protein C (OMIM Ref. No. 176860)

uses the endothelial cell protein C receptor (EPCR; 600646) as a coreceptor for cleavage of protease-activated receptor 1 (PAR1) on endothelial cells. Gene profiling demonstrated that PAR1 signaling could account for all activated protein C-induced protective genes, including the immunomodulatory monocyte chemoattractant protein-1 (MCP1; 158105), which was selectively induced by activation of PAR1, but not PAR2 (OMIM Ref. No. 600933). Thus, Riewald et al. (2002) concluded that the prototypical thrombin receptor is the target for EPCR-dependent APC signaling, suggesting a role for this receptor cascade in protection from sepsis. Animal model experiments lend further support to the function of F2R. Griffin et al. (2001) reported a role for Par1, a protease-activated G protein-coupled receptor for thrombin, in embryonic development. Approximately one-half of Par1 $-/-$ embryos died at midgestation with bleeding from multiple sites. Par1 is expressed in endothelial cells, and a Par1 transgene driven by an endothelial-specific promoter prevented death of Par1 $-/-$ embryos. Griffin et al. (2001) concluded that the coagulation cascade and PAR1 modulate endothelial cell function in developing blood vessels and that thrombin's actions on endothelial cells, rather than

on platelets, mesenchymal cells, or fibrinogen (see OMIM Ref. No. 134820), contribute to vascular development and hemostasis in the mouse embryo.

[10518] It is appreciated that the abovementioned animal model for F2R is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10519] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10520] Coughlin, S. R.; Vu, T.-K. H.; Hung, D. T.; Wheaton, V. I. : Characterization of a functional thrombin receptor: issues and opportunities. J. Clin. Invest. 89: 351-355, 1992. ; and

[10521] Riewald, M.; Petrovan, R. J.; Donner, A.; Mueller, B. M.; Ruf, W. : Activation of endothelial cell protease activated receptor 1 by the protein C pathway. Science 296: 1880-1882, 2002.

[10522] Further studies establishing the function and utilities of F2R are found in John Hopkins OMIM database record ID 187930, and in cited publications numbered 1750-175 and 5703-1756 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030671) is another VGAM140 host target gene. PTPRO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPRO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE, designated SEQ ID:25028, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10523] Another function of VGAM140 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030671), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO has been established by previous studies. To identify protein-tyrosine phosphatases (PTPases) involved in the oncogenic process leading to the development of pancreatic carcinoma, Wang et al. (1996) performed PCR on pooled poly(A)+ RNA from 9 human pancreatic carcinoma cell

lines using PTPase consensus oligonucleotide primers. One of the novel PCR products recovered was termed PCP2 (pancreatic carcinoma phosphatase-2) and was used to screen a human pancreatic adenocarcinoma cDNA library. The full sequence of PCP2 predicts a 1,430 amino acid protein consisting of a putative extracellular domain of 740 amino acids, a single transmembrane domain, and an intracellular domain of 666 amino acids. The intracellular region contains 2 tandemly repeated PTP catalytic domains with a high degree of identity to the catalytic domains of mouse PTP-kappa and PTP-mu. In addition to a signal peptide and 13 potential N-linked glycosylation sites, the extracellular domain contains a MAM (meprin/A5/PTP-mu) domain followed by 1 Ig-like repeat and 4 putative fibronectin type III repeats. The MAM domain, found in *Xenopus* A5 glycoprotein, meprin A, and meprin B, as well as in PTP-kappa and PTP-mu, may be involved in attachment to the cytoskeleton. PCP2, PTP-kappa, and PTP-mu appear to form a subfamily of MAM-containing receptor-like PTPs (RPTPs). PCP2 also contains the tripeptide HAV, implicated in cell-cell contact in the cadherins. By Northern blot analysis, Wang et al. (1996) demonstrated that the 5.5-kb PCP2 transcript is widely

distributed at varying levels, with very high expression in brain, skeletal muscle, and pancreas, but no expression in placenta or spleen. Wang et al. (1996) demonstrated tyrosine phosphatase activity using an in vitro pNPP assay. Subcellular localization using laser scanning immunofluorescence microscopy showed localization of PCP2 at intercellular adhesions and colocalization with beta-catenin and E-cadherin. Wang et al. (1996) hypothesized that PCP2 and other members of this subfamily of RPTPases may function as cell contact receptors that mediate and control cell-cell signals. Wang et al. (1997) used degenerate PCR to clone PTP-J, a member of the type II receptor PTPase family. The PTP-J cDNA encodes a 1,436-amino acid polypeptide that includes a single transmembrane domain and a cytoplasmic domain containing 2 tandemly repeated PTP catalytic domains. The presence of 2 PTP domains indicates that this gene is a member of the type II receptor PTPases. Northern blot analysis detected expression in skeletal muscle, heart, prostate, pancreas, and placenta. Wang et al. (1997) found that in lymphocytes or lymphoma cells, expression of PTP-J is downregulated following stimulation by either phorbol myristate acetate (PMA) or calcium ionophore, suggesting that PMA or cal-

cium signaling pathways may be involved in regulating the expression of PTP-J.

[10524] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10525] Wang, B.; Kishihara, K.; Zhang, D.; Hara, H.; Nomoto, K. : Molecular cloning and characterization of a novel human receptor protein tyrosine phosphatase gene, hPTP-J: down-regulation of gene expression by PMA and calcium ionophore in Jurkat T lymphoma cells. *Biochem. Biophys. Res. Commun.* 231: 77-81, 1997. ; and

[10526] Wang, H; Lian, Z; Lerch, M. M.; Chen, Z; Xie, W; Ullrich, A. : Characterization of PCP-2, a novel receptor protein tyrosine phosphatase of the MAM domain family. *Oncogene* 12: 2555-2562.

[10527] Further studies establishing the function and utilities of PTPRO are found in John Hopkins OMIM database record ID 602454, and in cited publications numbered 6323-6324 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sirtuin Silent Mating Type Information Regulation 2 Homolog 3 (*S. cerevisiae*) (SIRT3, Accession NM_012239) is another VGAM140 host target gene. SIRT3 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by SIRT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIRT3 BINDING SITE, designated SEQ ID:14545, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10528] Another function of VGAM140 is therefore inhibition of Sirtuin Silent Mating Type Information Regulation 2 Homolog 3 (*S. cerevisiae*) (SIRT3, Accession NM_012239), a gene which might function in telomeric silencing, cell cycle progression and chromosome stability. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIRT3. The function of SIRT3 has been established by previous studies. The yeast Sir2 protein (Shore et al., 1984) regulates epigenetic gene silencing and, as a possible antiaging effect, suppresses recombination of rDNA. Studies involving cobB, a bacterial Sir2-like gene, have suggested that Sir2 may encode a pyridine nucleotide transferase. By in silico and PCR-cloning techniques, Frye (1999) obtained cDNA sequences encoding 5 human

Sir2-like genes, which they called sirtuin-1 to -5 (SIRT1 to SIRT5). The SIRT1 (OMIM Ref. No. 604479) sequence has the closest homology to the *S. cerevisiae* Sir2 protein, while SIRT4 (OMIM Ref. No. 604482) and SIRT5 (OMIM Ref. No. 604483) more closely resemble prokaryotic sirtuin sequences. PCR analysis showed that the 5 human sirtuins are widely expressed in fetal and adult tissues. Recombinant human SIRT2 (OMIM Ref. No. 604480) was able to cause radioactivity to be transferred from (32P)NAD to bovine serum albumin (BSA). When a conserved histidine within SIRT2 was converted to tyrosine, the mutant recombinant protein was unable to transfer radioactivity from (32P)NAD to BSA. These results suggested that the sirtuins may function via mono-ADP-ribosylation of proteins. Tanny et al. (1999) showed that the yeast Sir2 protein can transfer labeled phosphate from nicotinamide adenine dinucleotide to itself and histones in vitro. A modified form of Sir2, which results from its automodification activity, was specifically recognized by anti-mono-ADP-ribose antibodies, suggesting that Sir2 is an ADP-ribosyltransferase. Mutation of a phylogenetically invariant histidine (his364 to tyr) in Sir2 abolished both its enzymatic activity in vitro and its silencing functions in

vivo. However, the mutant protein was associated with chromatin and other silencing factors in a manner similar to wildtype Sir2. These findings suggested that Sir2 contains an ADP-ribosyltransferase activity that is essential for its silencing function.

[10529] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10530] Tanny, J. C.; Dowd, G. J.; Huang, J.; Hilz, H.; Moazed, D. : An enzymatic activity in the yeast Sir2 protein that is essential for gene silencing. Cell 99: 735-745, 1999. ; and

[10531] Frye, R. A. : Characterization of five human cDNAs with homology to the yeast SIR2 gene: Sir2-like proteins (sirtuins) metabolize NAD and may have protein ADP-ribosyltransferase activity.

[10532] Further studies establishing the function and utilities of SIRT3 are found in John Hopkins OMIM database record ID 604481, and in cited publications numbered 5008, 504 and 5051 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 16 (monocarboxylic acid transporters), Member 1 (SLC16A1, Accession NM_003051) is another VGAM140 host target gene. SLC16A1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC16A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC16A1 BINDING SITE, designated SEQ ID:9014, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10533] Another function of VGAM140 is therefore inhibition of Solute Carrier Family 16 (monocarboxylic acid transporters), Member 1 (SLC16A1, Accession NM_003051), a gene which is a Proton-monocarboxylate cotransporter that transports lactate and pyruvate. Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC16A1. The function of SLC16A1 has been established by previous studies. The monocarboxylate transporter (MCT) mediates the movement of lactate and pyruvate across cell membranes (Garcia et al., 1994). Import and export of these substrates by tissues such as erythrocytes, muscle, intestine, and kidney are ascribed largely to the action of a proton-coupled MCT. Kim et al. (1992) cloned a cDNA for MCT1, which encodes a protein with 12 puta-

tive membrane-spanning regions; it was originally isolated by an expression cloning strategy designed to identify the mevalonate transporter in a mutant Chinese hamster ovary (CHO) cell line. The cloned mevalonate transporter turned out to be a mutant protein, designated Mev, that differed from its wildtype progenitor by 1 amino acid in the tenth membrane spanning region, which changed a phenylalanine (wildtype) to a cysteine (OMIM Ref. No. mutant). The finding that the wildtype cDNA did not elicit increased mevalonate transport in transfected cells suggested that the wildtype protein is a transporter for a molecule other than mevalonate. Indeed, subsequent studies by Garcia et al. (1994) showed that lactate, pyruvate, and related monocarboxylates can be transported by the wildtype molecule, designated MCT1 by them. This protein exhibits properties that resemble those of the erythrocyte MCT, including proton symport, trans acceleration, and sensitivity to alpha-cyanocinnamates. The amino acid sequence of MCT1 did not resemble that of any known protein, suggesting that MCT1 may represent a new class of solute carriers (solute carrier family 16). Garcia et al. (1994) used the hamster cDNA to isolate genomic cDNA clones for human MCT1. Comparison of the

human and hamster amino acid sequences demonstrated that the proteins are 86% identical. The gene for human MCT1, symbolized SLC16A1, was localized to 1p13.2–p12 by PCR analysis of panels of human/rodent cell hybrid lines and by fluorescence chromosomal in situ hybridization.

- [10534] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [10535] Garcia, C. K.; Goldstein, J. L.; Pathak, R. K.; Anderson, R. G. W.; Brown, M. S. : Molecular characterization of a membrane transporter for lactate, pyruvate, and other monocarboxylates: implications for the Cori cycle. *Cell* 76: 865–873, 1994. ; and
- [10536] Garcia, C. K.; Li, X.; Luna, J.; Francke, U. : cDNA cloning of the human monocarboxylate transporter 1 and chromosomal localization of the SLC16A1 locus to 1p13.2–p12. *Genomics* 23: 500–503.
- [10537] Further studies establishing the function and utilities of SLC16A1 are found in John Hopkins OMIM database record ID 600682, and in cited publications numbered 7130–7132 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Activator

of Basal Transcription 1 (ABT1, Accession NM_013375) is another VGAM140 host target gene. ABT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABT1 BINDING SITE, designated SEQ ID:15029, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10538] Another function of VGAM140 is therefore inhibition of Activator of Basal Transcription 1 (ABT1, Accession NM_013375). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABT1. CNIL (Accession NM_005776) is another VGAM140 host target gene. CNIL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNIL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNIL BINDING SITE, designated SEQ ID:12353, to the nucleotide sequence of VGAM140 RNA, herein designated

VGAM RNA, also designated SEQ ID:2851.

[10539] Another function of VGAM140 is therefore inhibition of CNIL (Accession NM_005776). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNIL. FLJ10876 (Accession NM_018254) is another VGAM140 host target gene. FLJ10876 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10876 BINDING SITE, designated SEQ ID:20220, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10540] Another function of VGAM140 is therefore inhibition of FLJ10876 (Accession NM_018254). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10876. FLJ14957 (Accession NM_032866) is another VGAM140 host target gene. FLJ14957 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14957, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14957 BINDING SITE, designated SEQ ID:26679, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10541] Another function of VGAM140 is therefore inhibition of FLJ14957 (Accession NM_032866). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14957. FLJ20174 (Accession NM_017699) is another VGAM140 host target gene. FLJ20174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20174 BINDING SITE, designated SEQ ID:19267, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10542] Another function of VGAM140 is therefore inhibition of FLJ20174 (Accession NM_017699). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ20174. FLJ20847 (Accession XM_170677) is another VGAM140 host target gene. FLJ20847 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20847, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20847 BINDING SITE, designated SEQ ID:45457, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10543] Another function of VGAM140 is therefore inhibition of FLJ20847 (Accession XM_170677). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20847. Glucosidase, Beta (bile acid) 2 (GBA2, Accession XM_048518) is another VGAM140 host target gene. GBA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GBA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBA2 BINDING SITE, designated SEQ ID:35178, to the nu-

cleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10544] Another function of VGAM140 is therefore inhibition of Glucosidase, Beta (bile acid) 2 (GBA2, Accession XM_048518). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBA2. KIAA0923 (Accession NM_014021) is another VGAM140 host target gene. KIAA0923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0923 BINDING SITE, designated SEQ ID:15241, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10545] Another function of VGAM140 is therefore inhibition of KIAA0923 (Accession NM_014021). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0923. KIAA0937 (Accession XM_166213) is another VGAM140 host target gene. KIAA0937 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0937 BINDING SITE, designated SEQ ID:44013, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10546] Another function of VGAM140 is therefore inhibition of KIAA0937 (Accession XM_166213). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0937. KIAA1203 (Accession XM_049683) is another VGAM140 host target gene. KIAA1203 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1203 BINDING SITE, designated SEQ ID:35468, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10547] Another function of VGAM140 is therefore inhibition of

KIAA1203 (Accession XM_049683). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1203. KIAA1796 (Accession XM_166146) is another VGAM140 host target gene. KIAA1796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1796 BINDING SITE, designated SEQ ID:43964, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10548] Another function of VGAM140 is therefore inhibition of KIAA1796 (Accession XM_166146). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1796. Transducer of ERBB2, 2 (TOB2, Accession XM_170995) is another VGAM140 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45765, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10549] Another function of VGAM140 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM_170995). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. TP53TG3 (Accession NM_015369) is another VGAM140 host target gene. TP53TG3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TP53TG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53TG3 BINDING SITE, designated SEQ ID:17669, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10550] Another function of VGAM140 is therefore inhibition of TP53TG3 (Accession NM_015369). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53TG3. LOC147671 (Accession XM_085844) is another VGAM140

host target gene. LOC147671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147671 BINDING SITE, designated SEQ ID:38377, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10551] Another function of VGAM140 is therefore inhibition of LOC147671 (Accession XM_085844). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147671. LOC253805 (Accession XM_172854) is another VGAM140 host target gene. LOC253805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253805 BINDING SITE, designated SEQ ID:46134, to the nucleotide sequence of VGAM140 RNA, herein designated VGAM RNA, also designated SEQ ID:2851.

[10552] Another function of VGAM140 is therefore inhibition of LOC253805 (Accession XM_172854). Accordingly, utilities of VGAM140 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253805. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 141 (VGAM141) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10553] VGAM141 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM141 was detected is described hereinabove with reference to Figs. 1–8.

[10554] VGAM141 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10555] VGAM141 gene encodes a VGAM141 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM141

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM141 precursor RNA is designated SEQ ID:127, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:127 is located at position 151833 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10556] VGAM141 precursor RNA folds onto itself, forming VGAM141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10557] An enzyme complex designated DICER COMPLEX, `dices` the VGAM141 folded precursor RNA into VGAM141 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 62%) nucleotide sequence of VGAM141 RNA is designated SEQ ID:2852, and is provided hereinbelow with reference to the sequence listing part.

[10558] VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM141 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10559] VGAM141 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM141 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM141 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10560] The complementary binding of VGAM141 RNA, herein designated VGAM RNA, to host target binding sites on VGAM141 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM141 host target RNA into VGAM141 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10561] It is appreciated that VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM141 host target genes. The mRNA of

each one of this plurality of VGAM141 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM141 RNA, herein designated VGAM RNA, and which when bound by VGAM141 RNA causes inhibition of translation of respective one or more VGAM141 host target proteins.

[10562] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM141 gene, herein designated VGAM GENE, on one or more VGAM141 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[10563] It is yet further appreciated that a function of VGAM141 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM141 correlate with, and may be deduced from, the identity of the host target genes which VGAM141 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10564] Nucleotide sequences of the VGAM141 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM141 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM141 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM141 are further described hereinbelow with reference to Table 1.

[10565] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM141 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM141 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10566] As mentioned hereinabove with reference to Fig. 1, a function of VGAM141 gene, herein designated VGAM is inhibition of expression of VGAM141 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM141 correlate with, and may be deduced from, the identity of the target genes which VGAM141 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10567] Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283) is a VGAM141 host target gene. TACC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TACC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TACC1 BINDING SITE, designated SEQ ID:12966, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10568] A function of VGAM141 is therefore inhibition of Trans-

forming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283). Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACC1. Trans-membrane, Prostate Androgen Induced RNA (TMEPAI, Accession NM_020182) is another VGAM141 host target gene. TMEPAI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMEPAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEPAI BINDING SITE, designated SEQ ID:21402, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10569] Another function of VGAM141 is therefore inhibition of Transmembrane, Prostate Androgen Induced RNA (TMEPAI, Accession NM_020182). Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEPAI. FLJ00026 (Accession XM_036307) is another VGAM141 host target gene. FLJ00026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ00026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00026 BINDING SITE, designated SEQ ID:32424, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10570] Another function of VGAM141 is therefore inhibition of FLJ00026 (Accession XM_036307). Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00026. FLJ11320 (Accession NM_018389) is another VGAM141 host target gene. FLJ11320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11320 BINDING SITE, designated SEQ ID:20428, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10571] Another function of VGAM141 is therefore inhibition of FLJ11320 (Accession NM_018389). Accordingly, utilities of

VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11320. FLJ14917 (Accession NM_032861) is another VGAM141 host target gene. FLJ14917 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14917 BINDING SITE, designated SEQ ID:26665, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10572] Another function of VGAM141 is therefore inhibition of FLJ14917 (Accession NM_032861). Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14917. FLJ22794 (Accession XM_166220) is another VGAM141 host target gene. FLJ22794 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22794 BINDING SITE,

designated SEQ ID:44024, to the nucleotide sequence of VGAM141 RNA, herein designated VGAM RNA, also designated SEQ ID:2852.

[10573] Another function of VGAM141 is therefore inhibition of FLJ22794 (Accession XM_166220). Accordingly, utilities of VGAM141 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22794. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 142 (VGAM142) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10574] VGAM142 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM142 was detected is described hereinabove with reference to Figs. 1–8.

[10575] VGAM142 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10576] VGAM142 gene encodes a VGAM142 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM142 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM142 precursor RNA is designated SEQ ID:128, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:128 is located at position 150841 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10577] VGAM142 precursor RNA folds onto itself, forming VGAM142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10578] An enzyme complex designated DICER COMPLEX, `dices` the VGAM142 folded precursor RNA into VGAM142 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM142 RNA is designated SEQ ID:2853, and is provided hereinbelow with reference to the sequence listing part.

[10579] VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM142 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10580] VGAM142 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM142 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM142 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10581] The complementary binding of VGAM142 RNA, herein designated VGAM RNA, to host target binding sites on VGAM142 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM142 host target RNA into VGAM142 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10582] It is appreciated that VGAM142 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM142 host target genes. The mRNA of each one of this plurality of VGAM142 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM142 RNA, herein designated VGAM RNA, and which when bound by VGAM142 RNA causes inhibition of translation of respective one or more VGAM142 host target proteins.

[10583] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM142 gene, herein designated VGAM GENE, on one or more VGAM142 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[10584] It is yet further appreciated that a function of VGAM142 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM142 correlate with, and may be deduced from, the identity of the host target genes which VGAM142 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10585] Nucleotide sequences of the VGAM142 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM142 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM142 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM142 are further described hereinbelow with reference to Table 1.

[10586] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM142 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM142 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10587] As mentioned hereinabove with reference to Fig. 1, a function of VGAM142 gene, herein designated VGAM is inhibition of expression of VGAM142 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM142 correlate with, and may be deduced from, the identity of the target genes which VGAM142 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10588] D10S170 (Accession NM_005436) is a VGAM142 host target gene. D10S170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D10S170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D10S170 BINDING SITE, designated SEQ ID:11919, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10589] A function of VGAM142 is therefore inhibition of D10S170 (Accession NM_005436), a gene which may provide a structural basis for generation of RET/PTC1 rearrangement. Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D10S170. The function of D10S170 has been established by previous studies. The PTC1 chimeric oncogene (RET/PTC1), which is detected only in papillary thyroid carcinoma (OMIM Ref. No. 188550), is generated by the fusion of the tyrosine kinase domain of the RET protooncogene (OMIM Ref. No. 164761) to the 5-prime terminal region of another gene, H4 (Donghi et al., 1989; Grieco et al., 1990; Sozzi et al., 1991). PTC1 oncogene occurs in as many as 30% of papillary thyroid carcinomas. The fusion gene is formed through intrachromosomal 'illegitimate' recombination involving an inversion of 10q (Pierotti et al., 1992). The H4 gene shows no significant homology to known genes, and the function of H4 protein is unknown. The RET protooncogene encodes a receptor-type tyrosine kinase, whose receptor is glial cell line-derived neurotrophic factor (OMIM Ref. No. 600837). Tong et al., (1995) showed that the putative leucine zipper in the N-terminal region

of H4 can mediate oligomerization of the PTC1 oncogene in vitro. Tong et al. (1997) demonstrated that the PTC1 oncogene forms a dimer in vivo, and the leucine zipper is responsible for this dimerization. Constitutive dimerization of the PTC1 oncogene appears to be essential for PTC1 transforming activity and constitutive oligomerization acquired by rearrangement or by point mutations may be a general mechanism for the activation of receptor tyrosine kinase oncogenes. See 601984 for discussion of the PTC3 chimeric oncogene. Nikiforova et al. (2000) asked whether, despite the great linear distance (30 mg) between RET and H4, recombination might be promoted by their proximity in the nucleus. Nikiforova et al. (2000) used 2-color FISH and 3-dimensional microscopy to map the positions of the RET and H4 loci within interphase nuclei. At least one pair of RET and H4 was juxtaposed in 35% of normal human thyroid cells and in 21% of peripheral blood lymphocytes, but only in 6% of normal mammary epithelial cells. Nikiforova et al. (2000) suggested that spatial contiguity of RET and H4 may provide a structural basis for generation of RET/PTC1 rearrangement by allowing a single radiation track to produce a double-strand break in each gene at the same site in the nucleus.

[10590] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10591] Pierotti, M. A.; Santoro, M.; Jenkins, R. B.; Sozzi, G.; Bongarzone, I.; Grieco, M.; Monzini, N.; Miozzo, M.; Hermann, M. A.; Fusco, A.; Hay, I. D.; Della Porta, G.; Vecchio, G. : Characterization of an inversion on the long arm of chromosome 10 juxtaposing D10S170 and RET and creating the oncogenic sequence RET/PTC. Proc. Nat. Acad. Sci. 89: 1616–1620, 1992. ; and

[10592] Nikiforova, M. N.; Stringer, J. R.; Blough, R.; Medvedovic, M.; Fagin, J. A.; Nikiforov, Y. E. : Proximity of chromosomal loci that participate in radiation-induced rearrangements in hu.

[10593] Further studies establishing the function and utilities of D10S170 are found in John Hopkins OMIM database record ID 601985, and in cited publications numbered 8897, 3532, 8898, 8899–890 and 1145 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hepatic Leukemia Factor (HLF, Accession NM_002126) is another VGAM142 host target gene. HLF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

HLF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLF BINDING SITE, designated SEQ ID:7905, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10594] Another function of VGAM142 is therefore inhibition of Hepatic Leukemia Factor (HLF, Accession NM_002126). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLF. Interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40) (IL12B, Accession NM_002187) is another VGAM142 host target gene. IL12B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL12B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL12B BINDING SITE, designated SEQ ID:7944, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10595] Another function of VGAM142 is therefore inhibition of

Interleukin 12B (natural killer cell stimulatory factor 2, cytotoxic lymphocyte maturation factor 2, p40) (IL12B, Accession NM_002187). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL12B. Interleukin 1 Receptor Accessory Protein (IL1RAP, Accession NM_002182) is another VGAM142 host target gene. IL1RAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1RAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RAP BINDING SITE, designated SEQ ID:7941, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10596] Another function of VGAM142 is therefore inhibition of Interleukin 1 Receptor Accessory Protein (IL1RAP, Accession NM_002182), a gene which may function as a membrane receptor. promotes heterophilic cellular adhesion. Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RAP. The function of IL1RAP has been

established by previous studies. Interleukin-1 (IL1; 147760, 147720) receptor accessory protein (OMIM Ref. No. IL1RAP) is a transmembrane protein that is required for IL1 signal transduction (Wesche et al., 1997). Huang et al. (1997) isolated a human IL1RAP cDNA, called IL1RAcP by them, by screening a placenta cDNA library with a mouse Il1rap cDNA. They found that treatment of cells with IL1 induced the formation of a complex containing IL1RAP and type I IL1 receptor (IL1RA; 147810). The serine/threonine kinase IRAK (OMIM Ref. No. 300283) was recruited to this complex through its association with IL1RAP. Overexpression of mutant IL1RAP proteins lacking the intracellular IRAK-binding domain prevented the recruitment of IRAK to the receptor complex. By fluorescence in situ hybridization and radiation hybrid analysis, Dale et al. (1998) mapped the IL1RAP gene to 3q28.

[10597] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10598] Huang, J.; Gao, X.; Li, S.; Cao, Z. : Recruitment of IRAK to the interleukin 1 receptor complex requires interleukin 1 receptor accessory protein. Proc. Nat. Acad. Sci. 94: 12829-12832, 1997. ; and

[10599] Wesche, H.; Korherr, C.; Kracht, M.; Falk, W.; Resch, K.; Martin, M. U. : The interleukin-1 receptor accessory protein (IL-1RAcP) is essential for IL-1-induced activation of interleukin.

[10600] Further studies establishing the function and utilities of IL1RAP are found in John Hopkins OMIM database record ID 602626, and in cited publications numbered 8562-8564 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sodium Channel, Nonvoltage-gated 1, Gamma (SCNN1G, Accession NM_001039) is another VGAM142 host target gene. SCNN1G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCNN1G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCNN1G BINDING SITE, designated SEQ ID:6706, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10601] Another function of VGAM142 is therefore inhibition of Sodium Channel, Nonvoltage-gated 1, Gamma (SCNN1G, Accession NM_001039). Accordingly, utilities of VGAM142

include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCNN1G. Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727) is another VGAM142 host target gene. SLC24A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC24A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC24A1 BINDING SITE, designated SEQ ID:11103, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10602] Another function of VGAM142 is therefore inhibition of Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727), a gene which is a critical component of the visual transduction cascade, controlling the calcium concentration of outer segments during light and darkness. Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC24A1. The function of SLC24A1 has been established by previous studies. By screening a human retinal

cDNA library using the entire bovine rod sodium/potassium/calcium (Na-Ca+K) exchanger cDNA as a probe, Tucker et al. (1998) cloned the human NCKX1 gene. Human NCKX1 codes for a protein of 1,081 amino acids that shows 64% overall identity with the bovine protein. The 2 sets of putative transmembrane domains and their short connecting loops showed 94% identity, while the extracellular loop at the amino terminus was only 59% identical. Tucker et al. (1998) determined the genomic structure of the NCKX1 gene and found 1 intron in the 5-prime untranslated region and 8 within the coding region. Exon length varies from 54 to 2,037 bp Using fluorescence in situ hybridization and analysis of a radiation hybrid panel, Tucker et al. (1998) mapped the NCKX1 gene to chromosome 15q22

[10603] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10604] Tucker, J. E.; Winkfein, R. J.; Cooper, C. B.; Schnetkamp, P. P. : cDNA cloning of the human retinal rod Na-Ca + K exchanger: comparison with a revised bovine sequence. Invest. Ophthal. Vis. Sci. 39: 435-440, 1998. ; and

[10605] Tucker, J. E.; Winkfein, R. J.; Murthy, S. K.; Friedman, J. S.;

Walter, M. A.; Demetrick, D. J.; Schnetkamp, P. P. M. :
Chromosomal localization and genomic organization of
the human retina.

[10606] Further studies establishing the function and utilities of
SLC24A1 are found in John Hopkins OMIM database
record ID 603617, and in cited publications numbered
7591–7592 listed in the bibliography section hereinbelow,
which are also hereby incorporated by reference. SWI/SNF
Related, Matrix Associated, Actin Dependent Regulator of
Chromatin, Subfamily C, Member 1 (SMARCC1, Accession
NM_003074) is another VGAM142 host target gene.
SMARCC1 BINDING SITE is HOST TARGET binding site
found in the 3' untranslated region of mRNA encoded by
SMARCC1, corresponding to a HOST TARGET binding site
such as BINDING SITE I, BINDING SITE II or BINDING SITE III.
Table 2 illustrates the complementarity of the nucleotide
sequences of SMARCC1 BINDING SITE, designated SEQ
ID:9040, to the nucleotide sequence of VGAM142 RNA,
herein designated VGAM RNA, also designated SEQ
ID:2853.

[10607] Another function of VGAM142 is therefore inhibition of
SWI/SNF Related, Matrix Associated, Actin Dependent
Regulator of Chromatin, Subfamily C, Member 1

(SMARCC1, Accession NM_003074), a gene which is involved in chromatin remodeling. Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCC1. The function of SMARCC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Zinc Finger Protein 192 (ZNF192, Accession NM_006298) is another VGAM142 host target gene. ZNF192 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF192 BINDING SITE, designated SEQ ID:12993, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10608] Another function of VGAM142 is therefore inhibition of Zinc Finger Protein 192 (ZNF192, Accession NM_006298). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF192. Chromosome 21 Open Reading

Frame 108 (C21orf108, Accession XM_114191) is another VGAM142 host target gene. C21orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf108 BINDING SITE, designated SEQ ID:42774, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10609] Another function of VGAM142 is therefore inhibition of Chromosome 21 Open Reading Frame 108 (C21orf108, Accession XM_114191). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf108. Chromosome 8 Open Reading Frame 7 (C8orf7, Accession XM_088376) is another VGAM142 host target gene. C8orf7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf7 BINDING SITE, designated SEQ

ID:39650, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10610] Another function of VGAM142 is therefore inhibition of Chromosome 8 Open Reading Frame 7 (C8orf7, Accession XM_088376). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf7. Calcium Homeostasis Endoplasmic Reticulum Protein (CHERP, Accession NM_006387) is another VGAM142 host target gene. CHERP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHERP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHERP BINDING SITE, designated SEQ ID:13092, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10611] Another function of VGAM142 is therefore inhibition of Calcium Homeostasis Endoplasmic Reticulum Protein (CHERP, Accession NM_006387). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with CHERP. FLJ12121 (Accession NM_024978) is another VGAM142 host target gene. FLJ12121 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ12121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12121 BINDING SITE, designated SEQ ID:24538, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10612] Another function of VGAM142 is therefore inhibition of FLJ12121 (Accession NM_024978). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12121. KIAA0475 (Accession NM_014864) is another VGAM142 host target gene. KIAA0475 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0475, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0475 BINDING SITE, designated SEQ ID:16952, to the nucleotide sequence of

VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10613] Another function of VGAM142 is therefore inhibition of KIAA0475 (Accession NM_014864). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0475. KIAA1317 (Accession XM_098368) is another VGAM142 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41630, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10614] Another function of VGAM142 is therefore inhibition of KIAA1317 (Accession XM_098368). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. KIAA1434 (Accession XM_045585) is another VGAM142 host target gene. KIAA1434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1434 BINDING SITE, designated SEQ ID:34488, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10615] Another function of VGAM142 is therefore inhibition of KIAA1434 (Accession XM_045585). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1434. KIAA1462 (Accession XM_166132) is another VGAM142 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43923, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10616] Another function of VGAM142 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities

of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. KIAA1829 (Accession XM_030378) is another VGAM142 host target gene. KIAA1829 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1829, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1829 BINDING SITE, designated SEQ ID:31034, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10617] Another function of VGAM142 is therefore inhibition of KIAA1829 (Accession XM_030378). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1829. Protein Tyrosine Phosphatase, Receptor Type, R (PTPRR, Accession NM_130846) is another VGAM142 host target gene. PTPRR BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTPRR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of PTPRR BINDING SITE, designated SEQ ID:28382, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10618] Another function of VGAM142 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, R (PTPRR, Accession NM_130846). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRR. Transcription Factor-like 5 (basic helix-loop-helix) (TCFL5, Accession NM_006602) is another VGAM142 host target gene. TCFL5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCFL5 BINDING SITE, designated SEQ ID:13381, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10619] Another function of VGAM142 is therefore inhibition of Transcription Factor-like 5 (basic helix-loop-helix) (TCFL5, Accession NM_006602). Accordingly, utilities of

VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL5. LOC146243 (Accession XM_096956) is another VGAM142 host target gene. LOC146243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146243 BINDING SITE, designated SEQ ID:40677, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10620] Another function of VGAM142 is therefore inhibition of LOC146243 (Accession XM_096956). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146243. LOC153129 (Accession XM_087606) is another VGAM142 host target gene. LOC153129 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153129, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC153129 BINDING SITE, designated SEQ ID:39360, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10621] Another function of VGAM142 is therefore inhibition of LOC153129 (Accession XM_087606). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153129. LOC202451 (Accession XM_117401) is another VGAM142 host target gene. LOC202451 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202451 BINDING SITE, designated SEQ ID:43441, to the nucleotide sequence of VGAM142 RNA, herein designated VGAM RNA, also designated SEQ ID:2853.

[10622] Another function of VGAM142 is therefore inhibition of LOC202451 (Accession XM_117401). Accordingly, utilities of VGAM142 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202451. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 143 (VGAM143) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10623] VGAM143 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM143 was detected is described hereinabove with reference to Figs. 1–8.

[10624] VGAM143 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10625] VGAM143 gene encodes a VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM143 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM143 precursor RNA is designated SEQ ID:129, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:129 is located at position 222208 relative to the genome of

Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10626] VGAM143 precursor RNA folds onto itself, forming VGAM143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10627] An enzyme complex designated DICER COMPLEX, `dices` the VGAM143 folded precursor RNA into VGAM143 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM143 RNA is designated SEQ ID:2854, and is provided hereinbelow with reference to the sequence listing part.

[10628] VGAM143 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM143 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[10629] VGAM143 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM143 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM143 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM143 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[10630] The complementary binding of VGAM143 RNA, herein designated VGAM RNA, to host target binding sites on VGAM143 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM143 host target RNA into VGAM143 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10631] It is appreciated that VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM143 host target genes. The mRNA of each one of this plurality of VGAM143 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM143 RNA, herein designated VGAM RNA, and which when bound by VGAM143 RNA causes inhibition of translation of respective one or more VGAM143

host target proteins.

[10632] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM143 gene, herein designated VGAM GENE, on one or more VGAM143 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10633] It is yet further appreciated that a function of VGAM143 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syn-

drome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM143 correlate with, and may be deduced from, the identity of the host target genes which VGAM143 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10634] Nucleotide sequences of the VGAM143 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM143 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM143 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM143 are further described hereinbelow with reference to Table 1.

[10635] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM143 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM143 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10636] As mentioned hereinabove with reference to Fig. 1, a function of VGAM143 gene, herein designated VGAM is inhibition of expression of VGAM143 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM143 correlate with, and may be deduced from, the identity of the target genes which VGAM143 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10637] Cullin 3 (CUL3, Accession NM_003590) is a VGAM143 host target gene. CUL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CUL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CUL3 BINDING SITE, designated SEQ ID:9643, to the nucleotide sequence of VGAM143 RNA, herein designated VGAM RNA, also designated SEQ ID:2854.

[10638] A function of VGAM143 is therefore inhibition of Cullin 3 (CUL3, Accession NM_003590), a gene which may target other proteins for ubiquitin-dependent proteolysis. Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CUL3. The function of CUL3 has been established by previous studies. Kipreos et al. (1996) identified a conserved gene family, designated cullins, with at least

5 members in nematodes, 6 in humans, and 3 in *S. cerevisiae*. See CUL1 (OMIM Ref. No. 603134). Human CUL3 is an ortholog of nematode *cul3*. Michel and Xiong (1998) identified human CUL3 cDNAs and reported that the predicted protein is 768 amino acids long. Ishikawa et al. (1998) isolated a CUL3 cDNA, KIAA0617, as 1 of 100 brain cDNAs encoding large proteins. Using RT-PCR, they found that CUL3 is expressed in several tissues. Du et al. (1998) identified CUL3 as a gene whose expression in human fibroblasts is induced by phorbol 12-myristate 13-acetate (PMA) and suppressed by salicylate. They reported that the sequences of the human and *C. elegans* *cul3* proteins share 46% identity. Northern blot analysis revealed that CUL3 is expressed as major 2.8- and minor 4.3-kb transcripts in various human tissues, with the highest levels in skeletal muscle and heart.

[10639] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10640] Du, M.; Sansores-Garcia, L.; Zu, Z.; Wu, K. K. : Cloning and expression analysis of a novel salicylate suppressible gene, Hs-CUL-3, a member of cullin/Cdc53 family. *J. Biol. Chem.* 273: 24289-24292, 1998. ; and

- [10641] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete seque.
- [10642] Further studies establishing the function and utilities of CUL3 are found in John Hopkins OMIM database record ID 603136, and in cited publications numbered 5063, 9440–944 and 5062 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BLOV1 (Accession XM_083866) is another VGAM143 host target gene. BLOV1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BLOV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLOV1 BINDING SITE, designated SEQ ID:37519, to the nucleotide sequence of VGAM143 RNA, herein designated VGAM RNA, also designated SEQ ID:2854.
- [10643] Another function of VGAM143 is therefore inhibition of BLOV1 (Accession XM_083866). Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLOV1.

FLJ10849 (Accession NM_018243) is another VGAM143 host target gene. FLJ10849 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10849, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10849 BINDING SITE, designated SEQ ID:20206, to the nucleotide sequence of VGAM143 RNA, herein designated VGAM RNA, also designated SEQ ID:2854.

[10644] Another function of VGAM143 is therefore inhibition of FLJ10849 (Accession NM_018243). Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10849. Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622) is another VGAM143 host target gene. MRPL35 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MRPL35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL35 BINDING SITE, designated SEQ ID:18731, to the nucleotide sequence of VGAM143 RNA,

herein designated VGAM RNA, also designated SEQ ID:2854.

- [10645] Another function of VGAM143 is therefore inhibition of Mitochondrial Ribosomal Protein L35 (MRPL35, Accession NM_016622). Accordingly, utilities of VGAM143 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL35. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 144 (VGAM144) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [10646] VGAM144 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM144 was detected is described hereinabove with reference to Figs. 1–8.
- [10647] VGAM144 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [10648] VGAM144 gene encodes a VGAM144 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM144 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM144 precursor RNA is designated SEQ ID:130, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:130 is located at position 93494 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10649] VGAM144 precursor RNA folds onto itself, forming VGAM144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10650] An enzyme complex designated DICER COMPLEX, `dices` the VGAM144 folded precursor RNA into VGAM144 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM144 RNA is designated SEQ ID:2855, and is provided hereinbelow with reference to the sequence listing part.

[10651] VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM144 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10652] VGAM144 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM144 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM144 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10653] The complementary binding of VGAM144 RNA, herein designated VGAM RNA, to host target binding sites on VGAM144 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM144 host target RNA into VGAM144 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10654] It is appreciated that VGAM144 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM144 host target genes. The mRNA of each one of this plurality of VGAM144 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM144 RNA, herein designated VGAM RNA, and which when bound by VGAM144 RNA causes inhibition of translation of respective one or more VGAM144 host target proteins.

[10655] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM144 gene, herein designated VGAM GENE, on one or more VGAM144 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[10656] It is yet further appreciated that a function of VGAM144 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM144 correlate with, and may be deduced from, the identity of the host target genes which VGAM144 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10657] Nucleotide sequences of the VGAM144 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM144 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM144 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM144 are further described hereinbelow with reference to Table 1.

[10658] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM144 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM144 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10659] As mentioned hereinabove with reference to Fig. 1, a function of VGAM144 gene, herein designated VGAM is inhibition of expression of VGAM144 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM144 correlate with, and may be deduced from, the identity of the target genes which VGAM144 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10660] Axonal Transport of Synaptic Vesicles (ATSV, Accession NM_004321) is a VGAM144 host target gene. ATSV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATSV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATSV BINDING SITE, designated SEQ ID:10520, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10661] A function of VGAM144 is therefore inhibition of Axonal Transport of Synaptic Vesicles (ATSV, Accession NM_004321), a gene which is a motor for anterograde axonal transport of synaptic vesicle precursors. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATSV. The function of ATSV has been established by previous studies. Kinesin-related proteins constitute a large superfamily of microtubule-dependent proteins that mediate specific and diverse motile processes, including intracellular transport and cell division. The human ATSV protein is a member of the kinesin family and shows 95% identity to the KIF1A protein of mouse (Okada et al., 1995). KIF1A is an anterograde motor protein that transports membranous organelles along axonal microtubules. Its cargo includes a subset of precursors for synaptic vesicles: synaptophysin (OMIM Ref. No. 313475), synaptotagmin (OMIM Ref. No. 185605), and Rab3A (OMIM Ref. No. 179490). Animal model experiments lend further support to the function of ATSV. The phenotype of KIF1A knockout mice includes motor and sensory disturbances, a reduction in the density of synaptic vesicles in nerve terminals, and accumulation of clear vesicles in nerve cell bodies

(Yonekawa et al., 1998). It can be hypothesized that ATSV (and KIF1A in the mouse) may play a critical role in the development of axonal neuropathies resulting from impaired axonal transport.

[10662] It is appreciated that the abovementioned animal model for ATSV is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10663] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10664] Okada, Y.; Yamazaki, H.; Sekine-Aizawa, Y.; Hirokawa, N. : The neuron-specific kinesin superfamily protein KIF1A is a unique monomeric motor for anterograde axonal transport of synaptic vesicle precursors. Cell 81: 769–780, 1995. ; and

[10665] Yonekawa, Y.; Harada, A.; Okada, Y.; Funakoshi, T.; Kanai, Y.; Takei, Y.; Terada, S.; Noda, T.; Hirokawa, N. : Defect in synaptic vesicle precursor transport and neuronal cell death in.

[10666] Further studies establishing the function and utilities of ATSV are found in John Hopkins OMIM database record ID 601255, and in cited publications numbered 9473–9479

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fanconi Anemia, Complementation Group A (FANCA, Accession NM_000135) is another VGAM144 host target gene. FANCA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FANCA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCA BINDING SITE, designated SEQ ID:5628, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10667] Another function of VGAM144 is therefore inhibition of Fanconi Anemia, Complementation Group A (FANCA, Accession NM_000135). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCA. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463) is another VGAM144 host target gene. HNRPDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11952, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10668] Another function of VGAM144 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL has been established by previous studies. Kamei et al. (1999) identified 2 isoforms of HNRPDL, which they called JKTBP1 and JKTBP2, corresponding to the 1.4- and 2.8-kb transcripts identified by Tsuchiya et al. (1998), respectively. The larger transcript predicts a 420-amino acid protein with a calculated molecular mass of approximately 46.4 kD. The JKTBP2 protein has a longer N terminus, and both proteins contain multiple potential sites for phosphorylation and arginine methylation. Northern blot analysis showed that both transcripts were expressed in all tissues examined,

although the amounts and ratios of the transcripts varied in different tissues. Three JKTBP transcripts greater than 2.8 kb were expressed in pancreas, spleen, and thymus. Western blot analysis of myeloid leukemia cells showed proteins of 38 and 53 kD. Tsuchiya et al. (1998) determined that recombinant HNRPDL interacted with both the double- and single-stranded forms of JKT41, an oligodeoxynucleotide corresponding to the cis-acting element in intron 9 of the MPO gene. Recombinant HNRPDL also interacted with poly(G) and poly(A), but not with poly(U) or poly(C). Transient expression of HNRPDL repressed expression of reporter genes located downstream of the intron 9 element of JKT41 or the intron 7 element of FERE27, another oligodeoxynucleotide corresponding to MPO.

[10669] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10670] Kamei, D.; Tsuchiya, N.; Yamazaki, M.; Meguro, H.; Yamada, M. : Two forms of expression and genomic structure of the human heterogeneous nuclear ribonucleoprotein D-like JKTBP gene (HNRPDL). *Gene* 228: 13-22, 1999.
; and

[10671] Tsuchiya, N.; Kamei, D.; Takano, A.; Matsui, T.; Yamada, M. : Cloning and characterization of a cDNA encoding a novel heterogeneous nuclear ribonucleoprotein-like protein and its expressio.

[10672] Further studies establishing the function and utilities of HNRPDL are found in John Hopkins OMIM database record ID 607137, and in cited publications numbered 6085–6087 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM_001560) is another VGAM144 host target gene. IL13RA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL13RA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL13RA1 BINDING SITE, designated SEQ ID:7282, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10673] Another function of VGAM144 is therefore inhibition of Interleukin 13 Receptor, Alpha 1 (IL13RA1, Accession NM_001560), a gene which binds il-13 with a low affinity.

together with il-4r- alpha can form a functional receptor for il-13. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL13RA1. The function of IL13RA1 has been established by previous studies. Interleukin-4 (IL4; 147780) and interleukin-13 (IL13; 147683) are 2 cytokines that are secreted by activated T cells and have similar effects on monocytes and B cells. Zurawski et al. (1993) demonstrated that the IL4 receptor (OMIM Ref. No. 147781) is a complex of at least 2 components. They described a mutant form of human IL4 that competitively antagonizes both human IL4 and human IL13. The amino acid sequences of IL4 and IL13 are approximately 30% homologous, and circular dichroism spectroscopy demonstrates that both proteins have a highly alpha-helical structure. IL13 competitively inhibited binding of IL4 to functional human IL4 receptors expressed on a cell line that responds to both IL4 and IL13. The binding of IL4 to an IL4-responsive cell line that does not respond to IL13, and the binding of IL4 to cloned IL4R ligand binding protein expressed on heterologous cells, were not inhibited by IL13. The results demonstrated that IL4 and IL13 share a receptor component that is important for signal trans-

duction. Hilton et al. (1996) reviewed these and other data suggesting a model of IL4 and IL13 receptor composition and function Heinzmann et al. (2000) determined that a variant of human IL13 (OMIM Ref. No. 147683), arg110 to gln (OMIM Ref. No. A4464G), associated with asthma in case-control populations from Britain and Japan (peak odds ratio (OR) = 2.31, 95% confidence interval, 1.33 – 4.00); the variant also predicted asthma and higher serum IL13 levels in a general, Japanese pediatric population. The authors referred to this variant as gln110 to arg. Immunohistochemistry demonstrated that both subunits of IL13R are prominently expressed in bronchial epithelium and smooth muscle from asthmatic subjects. Detailed molecular modeling analyses indicated that residue 110 of IL13 is important in the internal constitution of the ligand and crucial in ligand-receptor interaction. A noncoding variant of IL13R-alpha 1, 1398A-G, associated primarily with high IgE levels (OR = 3.38 in males, 1.10 in females) rather than asthma

[10674] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10675] Hilton, D. J.; Zhang, J.-G.; Metcalf, D.; Alexander, W. S.;

Nicola, N. A.; Willson, T. A. : Cloning and characterization of a binding subunit of the interleukin 13 receptor that is also a component of the interleukin 4 receptor. Proc. Nat. Acad. Sci. 93: 497–501, 1996. ; and

[10676] Heinzmann, H.; Mao, X.-Q.; Akaiwa, M.; Kreomer, R. T.; Gao, P.-S.; Ohshima, K.; Umeshita, R.; Abe, Y.; Braun, S.; Yamashita, T.; Roberts, M. H.; Sugimoto, R.; and 20 others : Genetic var.

[10677] Further studies establishing the function and utilities of IL13RA1 are found in John Hopkins OMIM database record ID 300119, and in cited publications numbered 10630–10631, 687, 1063 and 11592 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 1 Receptor Accessory Protein (IL1RAP, Accession NM_002182) is another VGAM144 host target gene. IL1RAP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL1RAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RAP BINDING SITE, designated SEQ ID:7940, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2855.

[10678] Another function of VGAM144 is therefore inhibition of Interleukin 1 Receptor Accessory Protein (IL1RAP, Accession NM_002182), a gene which may function as a membrane receptor. promotes heterophilic cellular adhesion. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RAP. The function of IL1RAP and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM142. Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450) is another VGAM144 host target gene. KLHL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL3 BINDING SITE, designated SEQ ID:42271, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10679] Another function of VGAM144 is therefore inhibition of Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450).

Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL3. Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540) is another VGAM144 host target gene. MAT1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAT1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAT1A BINDING SITE, designated SEQ ID:43666, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10680] Another function of VGAM144 is therefore inhibition of Methionine Adenosyltransferase I, Alpha (MAT1A, Accession XM_165540). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAT1A. N-myc Downstream Regulated Gene 1 (NDRG1, Accession XM_005243) is another VGAM144 host target gene. NDRG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NDRG1, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG1 BINDING SITE, designated SEQ ID:29965, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10681] Another function of VGAM144 is therefore inhibition of N-myc Downstream Regulated Gene 1 (NDRG1, Accession XM_005243), a gene which may have a growth inhibitory role. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG1. The function of NDRG1 has been established by previous studies. Using mRNA differential display analysis to compare expression in cells cultured in the presence of 1% or 20% oxygen, Park et al. (2000) determined that NDRG1, which they called PROXY1, is markedly upregulated in hypoxic cells. Northern and Western blot analyses showed that the 43-kD NDRG1 protein has a longer half-life than does the mRNA transcript and that the upregulation occurs through a heme protein-dependent pathway. Autosomal recessive peripheral neuropathies are relatively rare but are clinically more severe than autosomal dominant forms of Charcot-Marie-Tooth disease (CMT). The Lom form of hereditary motor and

sensory neuropathy (HMSNL; 601455), or CMT4D, is one such disorder. HMSNL shows features of Schwann cell dysfunction and a concomitant early axonal involvement, suggesting that impaired axon–glia interactions play a major role in its pathogenesis. Kalaydjieva et al. (1996) mapped the disease gene to 8q24.3, where closely related disease haplotypes and strong linkage disequilibrium suggested a single founder mutation. Kalaydjieva et al. (2000) reduced the HMSNL interval to 200 kb and characterized it by means of large–scale genomic sequencing. Sequence analysis of 2 genes located in the critical region, NDRG1 and WISP1 (OMIM Ref. No. 603398), identified the founder HMSNL mutation, a nonsense arg148–to–ter mutation (605262.0001) in the NDRG1 gene.

[10682] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10683] Kalaydjieva, L.; Gresham, D.; Gooding, R.; Heather, L.; Baas, F.; de Jonge, R.; Blechschmidt, K.; Angelicheva, D.; Chandler, D.; Worsley, P.; Rosenthal, A.; King, R. H. M.; Thomas, P. K. : N–myc downstream–regulated gene 1 is mutated in hereditary motor and sensory neuropathy–Lom. Am. J. Hum. Genet. 67: 47–58, 2000. ; and

[10684] Park, H.; Adams, M. A.; Lachat, P.; Bosman, F.; Pang, S. C.; Graham, C. H. : Hypoxia induces the expression of a 43-kDa protein (PROXY-1) in normal and malignant cells. Biochem. Bioph.

[10685] Further studies establishing the function and utilities of NDRG1 are found in John Hopkins OMIM database record ID 605262, and in cited publications numbered 1353-135 and 2318-2322 listed in the bibliography section herein-below, which are also hereby incorporated by reference. Solute Carrier Family 7 (cationic amino acid transporter, y⁺ system), Member 6 (SLC7A6, Accession NM_003983) is another VGAM144 host target gene. SLC7A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC7A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC7A6 BINDING SITE, designated SEQ ID:10126, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10686] Another function of VGAM144 is therefore inhibition of Solute Carrier Family 7 (cationic amino acid transporter,

y+ system), Member 6 (SLC7A6, Accession NM_003983), a gene which is involved in mediating amino acid transport. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC7A6. The function of SLC7A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM87. Transgelin 2 (TAGLN2, Accession NM_003564) is another VGAM144 host target gene. TAGLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAGLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAGLN2 BINDING SITE, designated SEQ ID:9620, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10687] Another function of VGAM144 is therefore inhibition of Transgelin 2 (TAGLN2, Accession NM_003564), a gene which is similar to transgelins and may be an actin-binding proteins. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with TAGLN2. The function of TAGLN2 has been established by previous studies. By sequencing cDNAs randomly selected from a cDNA library derived from a human immature myeloid cell line, Nagase et al. (1995) isolated a cDNA encoding TAGLN2, which they called KIAA0120. The deduced 199-amino acid TAGLN2 protein shares 69.7% amino acid sequence identity with rat neuronal protein NP25 over 195 amino acids. Northern blot analysis detected TAGLN2 expression in all 16 human tissues examined, with high expression in lung, liver, kidney, spleen, thymus, small intestine, colon, prostate, testis, ovary, placenta, and peripheral blood leukocytes, lower expression in skeletal muscle, pancreas, and heart, and lowest expression in brain. Using a somatic cell hybrid mapping panel, Nagase et al. (1995) determined that the TAGLN2 gene maps to either chromosome 1 or 8. Stanier et al. (1998) noted that an EST cluster representing the TAGLN2 gene had been mapped to 1q21-q25. By linkage analysis, Stanier et al. (1998) mapped the mouse Tagln2 gene to distal chromosome 1, between the Fcgr2 gene (OMIM Ref. No. 146790) and marker D1Mit149. Distal mouse chromosome 1 shows homology of synteny with human 1q21-q25.

[10688] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10689] Nagase, T.; Miyajima, N.; Tanaka, A.; Sazuka, T.; Seki, N.; Sato, S.; Tabata, S.; Ishikawa, K.; Kawarabayasi, Y.; Kotani, H.; Nomura, N. : Prediction of the coding sequences of unidentified human genes. III. The coding sequences of 40 new genes (KIAA0081–KIAA0120) deduced by analysis of cDNA clones from human cell line KG–1. DNA Res. 2: 37–43, 1995. ; and

[10690] Stanier, P.; Abu–Hayyeh, S.; Murdoch, J. N.; Eddleston, J.; Copp, A. J. : Paralogous Sm22–alpha (Tagln) genes map to mouse chromosomes 1 and 9: further evidence for a paralogous relatio.

[10691] Further studies establishing the function and utilities of TAGLN2 are found in John Hopkins OMIM database record ID 604634, and in cited publications numbered 108 and 7526 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600) is another VGAM144 host target gene. TCF3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by TCF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF3 BINDING SITE, designated SEQ ID:35005, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10692] Another function of VGAM144 is therefore inhibition of Transcription Factor 3 (E2A immunoglobulin enhancer binding factors E12/E47) (TCF3, Accession XM_047600), a gene which plays major roles in determining tissue-specific cell fate during embryogenesis. Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF3. The function of TCF3 has been established by previous studies. Expression of immunoglobulin genes depends on various sequence motifs in their enhancer and promoter regions. One class of such sequences is the 'E boxes,' which are found in both heavy and light chain enhancers. The kappa-E2 site has been shown to be important for light chain gene transcription. Studies have demonstrated that E boxes are binding sites for proteins. To isolate cDNAs encoding kappa-E2-binding proteins, Murre et al.

(1989) screened a cDNA expression library derived from a human B-cell lymphoma cell line (BJAB) with an oligonucleotide containing a trimerized kappa-E2 site. They identified a partial cDNA encoding a protein that they designated E12. Using the E12 cDNA to rescreen the BJAB cDNA library, Murre et al. (1989) isolated a partial cDNA encoding a protein that they designated E47. The authors showed that both E12 and E47 bind specifically to the kappa-E2 sequence. They demonstrated that E47 binds kappa-E2 as a dimer in vitro. Sequence analysis suggested that E12 and E47 are derived from a single gene, called E2A or TCF3, via alternative splicing. E12 contains a leucine zipper; the corresponding region of E47 was not cloned. Both the E12 and E47 proteins contain a region that is homologous to regions in MYOD (OMIM Ref. No. 159970), members of the MYC family (e.g., 190080), the Drosophila 'daughterless' gene product, and products of the Drosophila 'achaete-scute' and 'twist' gene families. The homologous regions have the potential to form 2 amphipathic helices separated by an intervening loop. The hydrophobic residues present in the helices are highly conserved. The authors demonstrated that this helix-loop-helix motif plays a crucial role in both dimerization

and DNA binding. Animal model experiments lend further support to the function of TCF3. Heterodimers between tissue-specific basic helix-loop-helix (bHLH) proteins and the products of the E2A gene play major roles in determining tissue-specific cell fate. The E2A gene gives rise to 2 proteins, E12 and E47, by differential splicing of E12- and E47-specific bHLH-encoding exons. Although they were initially identified in B cells as immunoglobulin enhancer-binding proteins, they were subsequently found to be present in most cell types. To understand the broad role of E2A in development, Zhuang et al. (1994) generated E2A mutant mice following homologous recombination in embryonic stem cells. Homozygous mutant mice developed to full term without apparent abnormalities, but then displayed a high rate of postnatal death. The surviving mice showed retarded postnatal growth. Detailed examination of hematopoiesis revealed that the homozygous mutant mice contained no B cells, whereas other lineages, including the T cell, granulocyte, macrophage, and erythroid lineages, were intact. The block to B-cell differentiation occurred before the immunoglobulin gene D(H)-J(H) rearrangement. Surprisingly, heterozygous embryos contained, on average, about half

as many B cells as did wildtype embryos, suggesting the existence of a counting mechanism that translates levels of E2A into numbers of B cells. Sun (1994) generated transgenic mice in which the Id1 gene (OMIM Ref. No. 600349) was constitutively overexpressed in the B-cell lineage. The product of this gene is an inhibitor of the DNA-binding activity of bHLH proteins such as the E2A gene product. The phenotype of these transgenic mice depicted severe defects in early B-cell development, suggesting that the bHLH proteins play pivotal roles in B-cell development and that the downregulation of Id1 gene expression is necessary for B cells to differentiate.

[10693] It is appreciated that the abovementioned animal model for TCF3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[10694] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10695] Murre, C.; McCaw, P. S.; Baltimore, D. : Cell 56: 777-783, 1989. ; and

[10696] Sun, X.-H. : Constitutive expression of the Id1 gene impairs mouse B cell development. Cell 79: 893-900, 1994.

[10697] Further studies establishing the function and utilities of TCF3 are found in John Hopkins OMIM database record ID 147141, and in cited publications numbered 11901–11903, 5203–5205, 11904–11907, 520 and 11351 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 20D7–FC4 (Accession XM_027578) is another VGAM144 host target gene. 20D7–FC4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by 20D7–FC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of 20D7–FC4 BINDING SITE, designated SEQ ID:30538, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10698] Another function of VGAM144 is therefore inhibition of 20D7–FC4 (Accession XM_027578). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with 20D7–FC4. Acetyl–Coenzyme A Synthetase 2 (ADP forming) (ACAS2, Accession NM_018677) is another VGAM144 host target gene. ACAS2 BINDING SITE1 and ACAS2 BIND–

ING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACAS2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACAS2 BINDING SITE1 and ACAS2 BINDING SITE2, designated SEQ ID:20751 and SEQ ID:29264 respectively, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10699] Another function of VGAM144 is therefore inhibition of Acetyl-Coenzyme A Synthetase 2 (ADP forming) (ACAS2, Accession NM_018677). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACAS2. Calsyntenin 3 (CLSTN3, Accession NM_014718) is another VGAM144 host target gene. CLSTN3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLSTN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN3 BINDING SITE, designated SEQ ID:16273, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2855.

[10700] Another function of VGAM144 is therefore inhibition of Calsyntenin 3 (CLSTN3, Accession NM_014718). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLSTN3. CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779) is another VGAM144 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNOT8 BINDING SITE, designated SEQ ID:11180, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10701] Another function of VGAM144 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. FBP17 (Accession XM_052666) is another VGAM144 host target gene. FBP17 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36047, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10702] Another function of VGAM144 is therefore inhibition of FBP17 (Accession XM_052666). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ12671 (Accession NM_030980) is another VGAM144 host target gene. FLJ12671 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12671 BINDING SITE, designated SEQ ID:25242, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10703] Another function of VGAM144 is therefore inhibition of

FLJ12671 (Accession NM_030980). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12671. FLJ20294 (Accession NM_017749) is another VGAM144 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294 BINDING SITE, designated SEQ ID:19345, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10704] Another function of VGAM144 is therefore inhibition of FLJ20294 (Accession NM_017749). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20294. FLJ23510 (Accession NM_024720) is another VGAM144 host target gene. FLJ23510 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23510, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ23510 BINDING SITE, designated SEQ ID:24051, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10705] Another function of VGAM144 is therefore inhibition of FLJ23510 (Accession NM_024720). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23510. Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903) is another VGAM144 host target gene. GABBR1 BINDING SITE1 and GABBR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GABBR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABBR1 BINDING SITE1 and GABBR1 BINDING SITE2, designated SEQ ID:22420 and SEQ ID:7204 respectively, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10706] Another function of VGAM144 is therefore inhibition of Gamma-aminobutyric Acid (GABA) B Receptor, 1 (GABBR1, Accession NM_021903). Accordingly, utilities of VGAM144

include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABBR1. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044) is another VGAM144 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:17397 and SEQ ID:30450 respectively, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10707] Another function of VGAM144 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA0703 (Accession NM_014861) is another VGAM144 host target gene. KIAA0703 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0703, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0703 BINDING SITE, designated SEQ ID:16929, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10708] Another function of VGAM144 is therefore inhibition of KIAA0703 (Accession NM_014861). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0703. KIAA1872 (Accession XM_031917) is another VGAM144 host target gene. KIAA1872 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31517, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10709] Another function of VGAM144 is therefore inhibition of KIAA1872 (Accession XM_031917). Accordingly, utilities

of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. LSFR2 (Accession XM_026945) is another VGAM144 host target gene. LSFR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LSFR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LSFR2 BINDING SITE, designated SEQ ID:30378, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10710] Another function of VGAM144 is therefore inhibition of LSFR2 (Accession XM_026945). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LSFR2. MGC10818 (Accession NM_030568) is another VGAM144 host target gene. MGC10818 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC10818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10818 BINDING

SITE, designated SEQ ID:24939, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10711] Another function of VGAM144 is therefore inhibition of MGC10818 (Accession NM_030568). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10818. RIP60 (Accession NM_013400) is another VGAM144 host target gene. RIP60 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RIP60, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIP60 BINDING SITE, designated SEQ ID:15059, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10712] Another function of VGAM144 is therefore inhibition of RIP60 (Accession NM_013400). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIP60. LOC122786 (Accession XM_058660) is another VGAM144 host target gene. LOC122786 BINDING SITE is HOST TAR-

GET binding site found in the 3' untranslated region of mRNA encoded by LOC122786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122786 BINDING SITE, designated SEQ ID:36699, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10713] Another function of VGAM144 is therefore inhibition of LOC122786 (Accession XM_058660). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122786. LOC147136 (Accession XM_085716) is another VGAM144 host target gene. LOC147136 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147136 BINDING SITE, designated SEQ ID:38299, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10714] Another function of VGAM144 is therefore inhibition of

LOC147136 (Accession XM_085716). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147136. LOC158267 (Accession XM_088528) is another VGAM144 host target gene. LOC158267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158267 BINDING SITE, designated SEQ ID:39792, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10715] Another function of VGAM144 is therefore inhibition of LOC158267 (Accession XM_088528). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158267. LOC164714 (Accession XM_104657) is another VGAM144 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42174, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10716] Another function of VGAM144 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC199796 (Accession XM_058994) is another VGAM144 host target gene. LOC199796 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199796 BINDING SITE, designated SEQ ID:36808, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10717] Another function of VGAM144 is therefore inhibition of LOC199796 (Accession XM_058994). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199796. LOC220522 (Accession XM_018306) is an-

other VGAM144 host target gene. LOC220522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220522 BINDING SITE, designated SEQ ID:30353, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10718] Another function of VGAM144 is therefore inhibition of LOC220522 (Accession XM_018306). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220522. LOC222031 (Accession XM_168371) is another VGAM144 host target gene. LOC222031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222031 BINDING SITE, designated SEQ ID:45134, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10719] Another function of VGAM144 is therefore inhibition of LOC222031 (Accession XM_168371). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222031. LOC253573 (Accession XM_173110) is another VGAM144 host target gene. LOC253573 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253573 BINDING SITE, designated SEQ ID:46365, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10720] Another function of VGAM144 is therefore inhibition of LOC253573 (Accession XM_173110). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253573. LOC91380 (Accession XM_038134) is another VGAM144 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91380, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32755, to the nucleotide sequence of VGAM144 RNA, herein designated VGAM RNA, also designated SEQ ID:2855.

[10721] Another function of VGAM144 is therefore inhibition of LOC91380 (Accession XM_038134). Accordingly, utilities of VGAM144 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 145 (VGAM145) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10722] VGAM145 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM145 was detected is described hereinabove with reference to Figs. 1–8.

[10723] VGAM145 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM145 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10724] VGAM145 gene encodes a VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM145 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM145 precursor RNA is designated SEQ ID:131, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:131 is located at position 279445 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10725] VGAM145 precursor RNA folds onto itself, forming VGAM145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10726] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM145 folded precursor RNA into VGAM145 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 50%) nucleotide sequence of VGAM145 RNA is designated SEQ ID:2856, and is provided hereinbelow with reference to the sequence listing part.

[10727] VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM145 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10728] VGAM145 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM145 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM145 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10729] The complementary binding of VGAM145 RNA, herein designated VGAM RNA, to host target binding sites on VGAM145 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM145 host target RNA into VGAM145 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10730] It is appreciated that VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM145 host target genes. The mRNA of each one of this plurality of VGAM145 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM145 RNA, herein designated VGAM RNA, and which when bound by VGAM145 RNA causes inhibition of translation of respective one or more VGAM145 host target proteins.

[10731] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM145 gene, herein designated VGAM GENE, on one or more VGAM145 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10732] It is yet further appreciated that a function of VGAM145 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM145 correlate with, and may be deduced from, the identity of the host target genes which VGAM145 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10733] Nucleotide sequences of the VGAM145 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM145 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM145 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM145 are further

described hereinbelow with reference to Table 1.

[10734] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM145 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM145 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10735] As mentioned hereinabove with reference to Fig. 1, a function of VGAM145 gene, herein designated VGAM is inhibition of expression of VGAM145 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM145 correlate with, and may be deduced from, the identity of the target genes which VGAM145 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10736] Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_001228) is a VGAM145 host target gene. CASP8 BINDING SITE1 through CASP8 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementar-

ity of the nucleotide sequences of CASP8 BINDING SITE1 through CASP8 BINDING SITE4, designated SEQ ID:6896, SEQ ID:27201, SEQ ID:27203 and SEQ ID:27204 respectively, to the nucleotide sequence of VGAM145 RNA, herein designated VGAM RNA, also designated SEQ ID:2856.

[10737] A function of VGAM145 is therefore inhibition of Caspase 8, Apoptosis-related Cysteine Protease (CASP8, Accession NM_001228), a gene which is an apoptosis-related caspase and an upstream component of Fas receptor and tumor necrosis factor (TNF) receptor-induced apoptosis. Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP8. The function of CASP8 has been established by previous studies. Expression of cDNAs that encode truncated polypeptides containing mostly expanded polyglutamine repeats, but not of those that encode the corresponding full-length proteins, has been shown to induce cell death by apoptosis. Such truncated proteins have been shown to form aggregates or inclusions (Ikeda et al., 1996). Sanchez et al. (1999) studied the role of caspases in polyglutamine-induced cell death in established cultures of primary cortical, striatal, and

cerebellar neurons from embryonic day 17 rat embryos, transfected with an expression construct encoding truncated ataxin-3 that contained 79 glutamine (Q79) residues. The authors showed that the apoptosis inhibitors Bcl2, CrmA, and a truncated Fas/APO1-associated death domain protein (FADD DN) inhibited polyglutamine repeat-induced neuronal cell death. A mutant Jurkat cell line specifically lacking caspase-8 was resistant to polyglutamine-induced cell death. Cells transfected with Q79 showed insoluble inclusions. Caspase-8 was recruited and activated by these Q79 inclusions. Western blot analysis revealed the presence of activated caspase-8 in the insoluble fraction of affected brain regions from Huntington disease (OMIM Ref. No. 143100) patients but not in those from controls. The authors suggested that caspase-8 has an essential role in Huntington-related neurodegenerative diseases. Animal model experiments lend further support to the function of CASP8. Varfolomeev et al. (1998) generated mice deficient in Casp8 by disrupting exons 1 and 2, which encode the N-terminal death effector domains (DEDs) that interact with MORT1/FADD (OMIM Ref. No. 602457). Whereas wildtype and heterozygous mice appeared normal, no homozygous mutant mice survived be-

yond approximately embryonic day 13.5. Histopathologic analysis revealed marked abdominal hyperemia with erythrocytosis in the liver, major blood vessels, capillaries, and other organs. Cardiac ventricular musculature was thin and similar to early mesenchyme. Colony forming assays showed that hemopoietic precursor cells were markedly reduced in the mutant mice. Immunoprecipitation and Western blot analysis indicated that fibroblasts from mutant mice responded normally to the noncytotoxic effects of tumor necrosis factor receptor (TNFR; 191190) and death receptor-3 (DR3, or TNFRSF12; 603366) stimulation, whereas wildtype fibroblasts were killed by TNF (OMIM Ref. No. 191160) treatment or FAS (TNFRSF6; 134637) cross-linking. Agents such as ultraviolet irradiation and protein kinase inhibitors were lethal for mutant and normal fibroblasts. Varfolomeev et al. (1998) concluded that CASP8 is necessary for death induction by receptors of the TNF/nerve growth factor (see OMIM Ref. No. NGFR; 162010) family and is vital in embryonal development.

[10738] It is appreciated that the abovementioned animal model for CASP8 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

[10739] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10740] Sanchez, I.; Xu, C.-J.; Juo, P.; Kakizaka, A.; Blenis, J.; Yuan, J. : Caspase-8 is required for cell death induced by expanded polyglutamine repeats. Neuron 22: 623-633, 1999. ; and

[10741] Varfolomeev, E. E.; Schuchmann, M.; Luria, V.; Chianilkulchai, N.; Beckmann, J. S.; Mett, I. L.; Rebrikov, D.; Brodianski, V. M.; Kemper, O. C.; Kollet, O.; Lapidot, T.; Soffer, D.; So.

[10742] Further studies establishing the function and utilities of CASP8 are found in John Hopkins OMIM database record ID 601763, and in sited publications numbered 6718, 7119, 1127 and 12074-6722 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ARNTL2 (Accession NM_020183) is another VGAM145 host target gene. ARNTL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARNTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of ARNTL2 BINDING SITE, designated SEQ ID:21411, to the nucleotide sequence of VGAM145 RNA, herein designated VGAM RNA, also designated SEQ ID:2856.

[10743] Another function of VGAM145 is therefore inhibition of ARNTL2 (Accession NM_020183). Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARNTL2. SEC24 Related Gene Family, Member B (*S. cerevisiae*) (SEC24B, Accession NM_006323) is another VGAM145 host target gene. SEC24B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC24B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC24B BINDING SITE, designated SEQ ID:13016, to the nucleotide sequence of VGAM145 RNA, herein designated VGAM RNA, also designated SEQ ID:2856.

[10744] Another function of VGAM145 is therefore inhibition of SEC24 Related Gene Family, Member B (*S. cerevisiae*) (SEC24B, Accession NM_006323). Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SEC24B. LOC138639 (Accession XM_059988) is another VGAM145 host target gene. LOC138639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC138639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138639 BINDING SITE, designated SEQ ID:37139, to the nucleotide sequence of VGAM145 RNA, herein designated VGAM RNA, also designated SEQ ID:2856.

[10745] Another function of VGAM145 is therefore inhibition of LOC138639 (Accession XM_059988). Accordingly, utilities of VGAM145 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138639. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 146 (VGAM146) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10746] VGAM146 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM146 was detected is described hereinabove with reference to Figs. 1–8.

[10747] VGAM146 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10748] VGAM146 gene encodes a VGAM146 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM146 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM146 precursor RNA is designated SEQ ID:132, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:132 is located at position 187726 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10749] VGAM146 precursor RNA folds onto itself, forming VGAM146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10750] An enzyme complex designated DICER COMPLEX, `dices` the VGAM146 folded precursor RNA into VGAM146 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM146 RNA is designated SEQ ID:2857, and is provided hereinbelow with reference to the sequence listing part.

[10751] VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM146 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[10752] VGAM146 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM146 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM146 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10753] The complementary binding of VGAM146 RNA, herein designated VGAM RNA, to host target binding sites on VGAM146 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM146 host target RNA into VGAM146 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10754] It is appreciated that VGAM146 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM146 host target genes. The mRNA of each one of this plurality of VGAM146 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM146 RNA, herein designated VGAM RNA, and which when bound by VGAM146 RNA causes inhibition of translation of respective one or more VGAM146 host target proteins.

[10755] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM146 gene, herein designated VGAM GENE, on one or more VGAM146 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10756] It is yet further appreciated that a function of VGAM146 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM146 correlate with, and may be deduced from, the identity of the host target genes which VGAM146 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [10757] Nucleotide sequences of the VGAM146 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM146 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM146 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM146 are further described hereinbelow with reference to Table 1.
- [10758] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM146 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM146 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [10759] As mentioned hereinabove with reference to Fig. 1, a function of VGAM146 gene, herein designated VGAM is inhibition of expression of VGAM146 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM146 correlate with, and may be deduced from, the identity of the target genes which VGAM146 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [10760] Bromodomain Adjacent to Zinc Finger Domain, 2B (BAZ2B,

Accession NM_013450) is a VGAM146 host target gene. BAZ2B BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BAZ2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAZ2B BINDING SITE, designated SEQ ID:15126, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10761] A function of VGAM146 is therefore inhibition of Bromodomain Adjacent to Zinc Finger Domain, 2B (BAZ2B, Accession NM_013450). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAZ2B. Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_080706) is another VGAM146 host target gene. TRPV1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TRPV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV1 BINDING SITE, designated SEQ

ID:28012, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10762] Another function of VGAM146 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_080706), a gene which functions as a receptor for capsaicin. Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV1. The function of TRPV1 has been established by previous studies. Chuang et al. (2001) demonstrated that bradykinin- or NGF-mediated potentiation of thermal sensitivity in vivo requires expression of VR1, a heat-activated ion channel on sensory neurons. Diminution of plasma membrane phosphatidylinositol-4,5,bisphosphate levels through antibody sequestration or PLC-mediated hydrolysis mimics the potentiating effects of bradykinin or NGF at the cellular level. Moreover, recruitment of PLC-gamma (OMIM Ref. No. 172420) to TRK-alpha (OMIM Ref. No. 191315) is essential for NGF-mediated potentiation of channel activity, and biochemical studies suggested that VR1 associates with this complex. Chuang et al. (2001) concluded that their studies delineate a biochemical

mechanism through which bradykinin and NGF produce hypersensitivity and might explain how the activation of PLC signaling systems regulates other members of the TRP channel family. Animal model experiments lend further support to the function of TRPV1. Caterina et al. (2000) generated mice deficient in VR1 by targeted disruption. VR1 $-/-$ mice were viable, fertile, and largely indistinguishable from wildtype littermates. Caterina et al. (2000) demonstrated that sensory neurons from mice lacking VR1 are severely deficient in their responses to vanilloid compounds, protons, or heat greater than 43 degrees C. VR1 $-/-$ mice showed normal responses to noxious mechanical stimuli but exhibited no vanilloid-evoked pain behavior, were impaired in the detection of painful heat, and showed little thermal hypersensitivity in the setting of inflammation. Thus, Caterina et al. (2000) concluded that VR1 is essential for selective modalities of pain sensation and for tissue injury-induced thermal hyperalgesia.

[10763] It is appreciated that the abovementioned animal model for TRPV1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[10764] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10765] Chuang, H.; Prescott, E. D.; Kong, H.; Shields, S.; Jordt, S.-E.; Basbaum, A. I.; Chao, M. V.; Julius, D. : Bradykinin and nerve growth factor release the capsaicin receptor from PtdIns(4,5)P₂-mediated inhibition. *Nature* 411: 957-962, 2001. ; and

[10766] Caterina, M. J.; Leffler, A.; Malmberg, A. B.; Martin, W. J.; Trafton, J.; Petersen-Zeltz, K. R.; Koltzenburg, M.; Basbaum, A. I.; Julius, D. : Impaired nociception and pain sensation in m.

[10767] Further studies establishing the function and utilities of TRPV1 are found in John Hopkins OMIM database record ID 602076, and in cited publications numbered 702, 1300-1301, 2236-1304, 1547-130 and 9434 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BNIP-S (Accession NM_138278) is another VGAM146 host target gene. BNIP-S BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BNIP-S, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of BNIP-S BINDING SITE, designated SEQ ID:28692, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10768] Another function of VGAM146 is therefore inhibition of BNIP-S (Accession NM_138278). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNIP-S. FLJ10661 (Accession NM_018172) is another VGAM146 host target gene. FLJ10661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10661 BINDING SITE, designated SEQ ID:19996, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10769] Another function of VGAM146 is therefore inhibition of FLJ10661 (Accession NM_018172). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10661. GW112 (Accession NM_006418) is another VGAM146 host

target gene. GW112 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GW112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GW112 BINDING SITE, designated SEQ ID:13128, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10770] Another function of VGAM146 is therefore inhibition of GW112 (Accession NM_006418). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GW112. MGC10812 (Accession NM_031425) is another VGAM146 host target gene. MGC10812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10812 BINDING SITE, designated SEQ ID:25409, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10771] Another function of VGAM146 is therefore inhibition of MGC10812 (Accession NM_031425). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10812. MGC16279 (Accession NM_032916) is another VGAM146 host target gene. MGC16279 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC16279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC16279 BINDING SITE, designated SEQ ID:26731, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10772] Another function of VGAM146 is therefore inhibition of MGC16279 (Accession NM_032916). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC16279. PME-1 (Accession NM_016147) is another VGAM146 host target gene. PME-1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PME-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PME-1 BINDING SITE, designated SEQ ID:18233, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10773] Another function of VGAM146 is therefore inhibition of PME-1 (Accession NM_016147). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PME-1. Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564) is another VGAM146 host target gene. SLC39A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC39A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC39A3 BINDING SITE, designated SEQ ID:29360, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10774] Another function of VGAM146 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564). Accordingly, utilities of

VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC39A3. LOC158490 (Accession XM_088585) is another VGAM146 host target gene. LOC158490 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158490 BINDING SITE, designated SEQ ID:39850, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10775] Another function of VGAM146 is therefore inhibition of LOC158490 (Accession XM_088585). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158490. LOC220073 (Accession XM_167847) is another VGAM146 host target gene. LOC220073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220073 BINDING SITE, designated SEQ ID:44876, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10776] Another function of VGAM146 is therefore inhibition of LOC220073 (Accession XM_167847). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220073. LOC90630 (Accession XM_033046) is another VGAM146 host target gene. LOC90630 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90630 BINDING SITE, designated SEQ ID:31826, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10777] Another function of VGAM146 is therefore inhibition of LOC90630 (Accession XM_033046). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90630. LOC91069 (Accession XM_035824) is another VGAM146 host target gene. LOC91069 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91069 BINDING SITE, designated SEQ ID:32348, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10778] Another function of VGAM146 is therefore inhibition of LOC91069 (Accession XM_035824). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91069. LOC92095 (Accession XM_042811) is another VGAM146 host target gene. LOC92095 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92095 BINDING SITE, designated SEQ ID:33774, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10779] Another function of VGAM146 is therefore inhibition of

LOC92095 (Accession XM_042811). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92095. LOC92096 (Accession XM_042812) is another VGAM146 host target gene. LOC92096 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92096 BINDING SITE, designated SEQ ID:33778, to the nucleotide sequence of VGAM146 RNA, herein designated VGAM RNA, also designated SEQ ID:2857.

[10780] Another function of VGAM146 is therefore inhibition of LOC92096 (Accession XM_042812). Accordingly, utilities of VGAM146 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92096. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 147 (VGAM147) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[10781] VGAM147 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM147 was detected is described hereinabove with reference to Figs. 1–8.

[10782] VGAM147 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10783] VGAM147 gene encodes a VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM147 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM147 precursor RNA is designated SEQ ID:133, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:133 is located at position 82267 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10784] VGAM147 precursor RNA folds onto itself, forming VGAM147 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[10785] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM147 folded precursor RNA into VGAM147 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 60%) nucleotide se-
quence of VGAM147 RNA is designated SEQ ID:2858, and
is provided hereinbelow with reference to the sequence
listing part.

[10786] VGAM147 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM147 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM147 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10787] VGAM147 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM147 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM147 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10788] The complementary binding of VGAM147 RNA, herein designated VGAM RNA, to host target binding sites on VGAM147 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM147 host target RNA into VGAM147 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10789] It is appreciated that VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM147 host target genes. The mRNA of each one of this plurality of VGAM147 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM147 RNA, herein designated VGAM RNA, and which when bound by VGAM147 RNA causes inhibition of translation of respective one or more VGAM147 host target proteins.

[10790] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM147 gene, herein designated VGAM GENE, on one or more VGAM147 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10791] It is yet further appreciated that a function of VGAM147 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM147 correlate with, and may be deduced from, the identity of the host target genes which VGAM147 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[10792] Nucleotide sequences of the VGAM147 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM147 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM147 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM147 are further described hereinbelow with reference to Table 1.

[10793] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM147 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM147 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10794] As mentioned hereinabove with reference to Fig. 1, a function of VGAM147 gene, herein designated VGAM is inhibition of expression of VGAM147 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM147 correlate with, and may be deduced from, the identity of the target genes which VGAM147 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[10795] Lysyl Oxidase-like 2 (LOXL2, Accession NM_002318) is a VGAM147 host target gene. LOXL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOXL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL2 BINDING SITE, designated SEQ ID:8133, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10796] A function of VGAM147 is therefore inhibition of Lysyl Oxidase-like 2 (LOXL2, Accession NM_002318), a gene which may have roles in senescence and cell adhesion. Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOXL2. The function of LOXL2 has been established by previous studies. LOXL2 is a member of the lysyl oxidase (LO; 153455) gene family. LO is an extracellular, copper-dependent enzyme that initiates the cross-linking of collagens and elastin by catalyzing the oxidative deamination of peptidyl lysine to alpha-aminoaldehydic-delta-semialdehyde. Members of the LO family have

diverse functions, including tumor suppression and cell adhesion and senescence Saito et al. (1997) used PCR and 5-prime RACE to obtain a full-length cDNA encoding LOXL2. The predicted 774-amino acid LOXL2 protein contains 3 potential N-linked glycosylation sites and 4 scavenger receptor cysteine-rich (SRCR) domains, which are involved in binding to other cell surface or extracellular molecules. LOXL2 also contains residues conserved among copper-binding proteins. In vitro translation produced an 87-kD LOXL2 protein. Northern blot analysis detected a 3.65-kb LOXL2 transcript in adherent tumor cell lines but not in suspension cell lines. Using cultured fibroblasts, Saito et al. (1997) demonstrated that LOXL2 expression is upregulated in senescent fibroblasts, induced by transforming growth factor beta-1 (OMIM Ref. No. 190180) and indomethacin, and inhibited by phorbol ester and retinoic acid. They concluded that LOXL2 is an extracellular matrix component that may be specifically involved in cell adhesion and senescence

[10797] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10798] Saito, H.; Papaconstantinou, J.; Sato, H.; Goldstein, S. :

Regulation of a novel gene encoding a lysyl oxidase-related protein in cellular adhesion and senescence. J. Biol. Chem. 272: 8157-8160, 1997. ; and

[10799] Saito, H.; Papaconstantinou, J.; Sato, H.; Goldstein, S. : Regulation of a novel gene encoding a lysyl oxidase-related protein in cellular adhesion and senescence. J. Biol. Chem. 272: 8157.

[10800] Further studies establishing the function and utilities of LOXL2 are found in John Hopkins OMIM database record ID 606663, and in cited publications numbered 6280-6281, 639 and 6450 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM147 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32197, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10801] Another function of VGAM147 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Solute Carrier Family 22 (organic cation transporter), Member 5 (SLC22A5, Accession NM_003060) is another VGAM147 host target gene. SLC22A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC22A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC22A5 BINDING SITE, designated SEQ ID:9026, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10802] Another function of VGAM147 is therefore inhibition of Solute Carrier Family 22 (organic cation transporter), Member 5 (SLC22A5, Accession NM_003060). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC22A5. KIAA1872 (Accession XM_031917) is another VGAM147 host target gene. KIAA1872 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31520, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10803] Another function of VGAM147 is therefore inhibition of KIAA1872 (Accession XM_031917). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. MGC3248 (Accession NM_032486) is another VGAM147 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26238, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10804] Another function of VGAM147 is therefore inhibition of

MGC3248 (Accession NM_032486). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. PEPP3 (Accession NM_014935) is another VGAM147 host target gene. PEPP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEPP3 BINDING SITE, designated SEQ ID:17235, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10805] Another function of VGAM147 is therefore inhibition of PEPP3 (Accession NM_014935). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEPP3. LOC157349 (Accession XM_088298) is another VGAM147 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:17236, to the nucleotide sequence of VGAM RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

tarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39597, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10806] Another function of VGAM147 is therefore inhibition of LOC157349 (Accession XM_088298). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. LOC163231 (Accession XM_092094) is another VGAM147 host target gene. LOC163231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163231 BINDING SITE, designated SEQ ID:40099, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10807] Another function of VGAM147 is therefore inhibition of LOC163231 (Accession XM_092094). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163231. LOC255527 (Accession XM_173026) is an-

other VGAM147 host target gene. LOC255527 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255527, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255527 BINDING SITE, designated SEQ ID:46294, to the nucleotide sequence of VGAM147 RNA, herein designated VGAM RNA, also designated SEQ ID:2858.

[10808] Another function of VGAM147 is therefore inhibition of LOC255527 (Accession XM_173026). Accordingly, utilities of VGAM147 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255527. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 148 (VGAM148) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10809] VGAM148 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM148 was detected is described

hereinabove with reference to Figs. 1–8.

[10810] VGAM148 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10811] VGAM148 gene encodes a VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM148 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM148 precursor RNA is designated SEQ ID:134, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:134 is located at position 164623 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10812] VGAM148 precursor RNA folds onto itself, forming VGAM148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10813] An enzyme complex designated DICER COMPLEX, `dices` the VGAM148 folded precursor RNA into VGAM148 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM148 RNA is designated SEQ ID:2859, and is provided hereinbelow with reference to the sequence listing part.

[10814] VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM148 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10815] VGAM148 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM148 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM148 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10816] The complementary binding of VGAM148 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM148 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM148 host target RNA into VGAM148 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10817] It is appreciated that VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM148 host target genes. The mRNA of each one of this plurality of VGAM148 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM148 RNA, herein designated VGAM RNA, and which when bound by VGAM148 RNA causes inhibition of translation of respective one or more VGAM148 host target proteins.

[10818] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM148 gene, herein designated VGAM GENE, on one or more VGAM148 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10819] It is yet further appreciated that a function of VGAM148 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM148 correlate with, and may be deduced from, the identity of the host target genes which VGAM148 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10820] Nucleotide sequences of the VGAM148 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM148 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM148 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM148 are further described hereinbelow with reference to Table 1.

[10821] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM148 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM148 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10822] As mentioned hereinabove with reference to Fig. 1, a function of VGAM148 gene, herein designated VGAM is inhibition of expression of VGAM148 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM148 correlate with, and may be deduced from, the identity of the target genes which VGAM148 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10823] Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_001224) is a VGAM148

host target gene. CASP2 BINDING SITE1 through CASP2 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CASP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP2 BINDING SITE1 through CASP2 BINDING SITE4, designated SEQ ID:6891, SEQ ID:26854, SEQ ID:26859 and SEQ ID:26864 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10824] A function of VGAM148 is therefore inhibition of Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_001224), a gene which involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP2. The function of CASP2 has been established by previous studies. Lassus et al. (2002) found that cytotoxic stress causes activation of caspase-2 and that this caspase is required for the permeabilization of mitochondria. Caspase-2 is required for

stress-induced apoptosis and for release of cytochrome c and Smac (OMIM Ref. No. 605219) from mitochondria and for translocation of Bax from the cytoplasm to mitochondria. Animal model experiments lend further support to the function of CASP2. To evaluate the requirement for caspase-2 in various aspects of apoptosis, Bergeron et al. (1998) generated caspase-2-deficient mice. Excess numbers of the germ cells were 'endowed' in ovaries of mutant mice, and the oocytes were resistant to cell death following exposure to chemotherapeutic drugs. Apoptosis mediated by granzyme B (OMIM Ref. No. 123910) and perforin (OMIM Ref. No. 170280) was defective in caspase-2-deficient B lymphoblasts. In contrast, cell death of motor neurons during development was accelerated in caspase-2-deficient mice. In addition, caspase-2-deficient sympathetic neurons underwent apoptosis more effectively than wildtype neurons when deprived of nerve growth factor. Thus, caspase-2 acts as both a positive and a negative cell death effector, depending upon cell lineage and stage of development.

[10825] It is appreciated that the abovementioned animal model for CASP2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

[10826] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10827] Bergeron, L.; Perez, G. I.; Macdonald, G.; Shi, L.; Sun, Y.; Jurisicova, A.; Varmuza, S.; Latham, K. E.; Flaws, J. A.; Salter, J. C. M.; Hara, H.; Moskowitz, M. A.; Li, E.; Greenberg, A.; Tilly, J. L.; Yuan, J. : Defects in regulation of apoptosis in caspase-2-deficient mice. *Genes Dev.* 12: 1304-1314, 1998. ; and

[10828] Lassus, P.; Opitz-Araya, X.; Lazebnik, Y. : Requirement for caspase-2 in stress-induced apoptosis before mitochondrial permeabilization. *Science* 297: 1352-1354, 2002.

[10829] Further studies establishing the function and utilities of CASP2 are found in John Hopkins OMIM database record ID 600639, and in sited publications numbered 7129, 7567, 7573-757 and 7126 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Angiomotin (AMOT, Accession NM_133265) is another VGAM148 host target gene. AMOT BINDING SITE1 and AMOT BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AMOT, corresponding to HOST TARGET binding sites such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AMOT BINDING SITE1 and AMOT BINDING SITE2, designated SEQ ID:28410 and SEQ ID:28418 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10830] Another function of VGAM148 is therefore inhibition of Angiomotin (AMOT, Accession NM_133265). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AMOT. Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM_016348) is another VGAM148 host target gene. C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C5orf4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2, designated SEQ ID:18475 and SEQ ID:15570 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10831] Another function of VGAM148 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM_016348). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. FLJ12985 (Accession NM_024924) is another VGAM148 host target gene. FLJ12985 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12985, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12985 BINDING SITE, designated SEQ ID:24464, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10832] Another function of VGAM148 is therefore inhibition of FLJ12985 (Accession NM_024924). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12985. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM148 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites

found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:28926 and SEQ ID:17404 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10833] Another function of VGAM148 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA0125 (Accession NM_014792) is another VGAM148 host target gene. KIAA0125 BINDING SITE1 through KIAA0125 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0125, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0125 BINDING SITE1 through KIAA0125 BINDING SITE3, designated SEQ

ID:16691, SEQ ID:30345 and SEQ ID:35403 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10834] Another function of VGAM148 is therefore inhibition of KIAA0125 (Accession NM_014792). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0125. Paternally Expressed 10 (PEG10, Accession NM_015068) is another VGAM148 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17434, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10835] Another function of VGAM148 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM_015068). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. PRP8 Pre-mRNA Processing Factor

8 Homolog (yeast) (PRPF8, Accession XM_028335) is another VGAM148 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30677, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10836] Another function of VGAM148 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM_028335). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRPF8. PRTD-NY3 (Accession NM_030924) is another VGAM148 host target gene. PRTD-NY3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRTD-NY3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRTD-NY3 BINDING SITE, designated SEQ ID:25193, to the nucleotide se-

quence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10837] Another function of VGAM148 is therefore inhibition of PRTD-NY3 (Accession NM_030924). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRTD-NY3. RAI (Accession NM_006663) is another VGAM148 host target gene. RAI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI BINDING SITE, designated SEQ ID:13468, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10838] Another function of VGAM148 is therefore inhibition of RAI (Accession NM_006663). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI. Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869) is another VGAM148 host target gene. SEZ6 BINDING SITE1 and SEZ6 BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by SEZ6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEZ6 BINDING SITE1 and SEZ6 BINDING SITE2, designated SEQ ID:36771 and SEQ ID:36772 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10839] Another function of VGAM148 is therefore inhibition of Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEZ6. LOC146227 (Accession XM_085374) is another VGAM148 host target gene. LOC146227 BINDING SITE1 through LOC146227 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC146227, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146227 BINDING SITE1 through LOC146227 BINDING SITE4, designated SEQ ID:38084,

SEQ ID:38085, SEQ ID:38086 and SEQ ID:40774 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10840] Another function of VGAM148 is therefore inhibition of LOC146227 (Accession XM_085374). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146227. LOC150333 (Accession XM_097874) is another VGAM148 host target gene. LOC150333 BINDING SITE1 and LOC150333 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC150333, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150333 BINDING SITE1 and LOC150333 BINDING SITE2, designated SEQ ID:41197 and SEQ ID:41199 respectively, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10841] Another function of VGAM148 is therefore inhibition of LOC150333 (Accession XM_097874). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC150333. LOC153688 (Accession XM_098416) is another VGAM148 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41656, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10842] Another function of VGAM148 is therefore inhibition of LOC153688 (Accession XM_098416). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. LOC157653 (Accession XM_088353) is another VGAM148 host target gene. LOC157653 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC157653, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157653 BINDING SITE, designated SEQ ID:39632, to

the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10843] Another function of VGAM148 is therefore inhibition of LOC157653 (Accession XM_088353). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157653. LOC219404 (Accession XM_167909) is another VGAM148 host target gene. LOC219404 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219404, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219404 BINDING SITE, designated SEQ ID:44910, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10844] Another function of VGAM148 is therefore inhibition of LOC219404 (Accession XM_167909). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219404. LOC221468 (Accession NM_145316) is another VGAM148 host target gene. LOC221468 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC221468, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221468 BINDING SITE, designated SEQ ID:29827, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10845] Another function of VGAM148 is therefore inhibition of LOC221468 (Accession NM_145316). Accordingly, utilities of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221468. LOC255624 (Accession XM_170531) is another VGAM148 host target gene. LOC255624 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255624, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255624 BINDING SITE, designated SEQ ID:45352, to the nucleotide sequence of VGAM148 RNA, herein designated VGAM RNA, also designated SEQ ID:2859.

[10846] Another function of VGAM148 is therefore inhibition of LOC255624 (Accession XM_170531). Accordingly, utilities

of VGAM148 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255624. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 149 (VGAM149) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10847] VGAM149 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM149 was detected is described hereinabove with reference to Figs. 1–8.

[10848] VGAM149 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10849] VGAM149 gene encodes a VGAM149 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM149 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM149 precursor RNA is designated SEQ ID:135, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:135 is located at position 68772 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10850] VGAM149 precursor RNA folds onto itself, forming VGAM149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10851] An enzyme complex designated DICER COMPLEX, `dices` the VGAM149 folded precursor RNA into VGAM149 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide se-

quence of VGAM149 RNA is designated SEQ ID:2860, and is provided hereinbelow with reference to the sequence listing part.

[10852] VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM149 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[10853] VGAM149 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM149 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM149 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10854] The complementary binding of VGAM149 RNA, herein designated VGAM RNA, to host target binding sites on VGAM149 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM149 host target RNA into VGAM149 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10855] It is appreciated that VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM149 host target genes. The mRNA of each one of this plurality of VGAM149 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM149 RNA, herein designated VGAM RNA, and which when bound by VGAM149 RNA causes inhibition of translation of respective one or more VGAM149 host target proteins.

[10856] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM149 gene, herein designated VGAM GENE, on one or more VGAM149 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10857] It is yet further appreciated that a function of VGAM149 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM149 correlate with, and may be deduced from, the identity of the host target genes which VGAM149 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10858] Nucleotide sequences of the VGAM149 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM149 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM149 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM149 are further described hereinbelow with reference to Table 1.

[10859] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM149 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM149 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[10860] As mentioned hereinabove with reference to Fig. 1, a function of VGAM149 gene, herein designated VGAM is inhibition of expression of VGAM149 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM149 correlate with, and may be deduced from, the identity of the target genes which VGAM149 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10861] Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395) is a VGAM149 host target gene. DYRK1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28159, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10862] A function of VGAM149 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395), a gene which regu-

lates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Glucosaminyl (N-acetyl) Transferase 1, Core 2 (beta-1,6-N-acetylglucosaminyltransferase) (GCNT1, Accession NM_001490) is another VGAM149 host target gene. GCNT1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GCNT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GCNT1 BINDING SITE, designated SEQ ID:7237, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10863] Another function of VGAM149 is therefore inhibition of Glucosaminyl (N-acetyl) Transferase 1, Core 2 (beta-1,6-N-acetylglucosaminyltransferase) (GCNT1, Accession NM_001490), a gene which forms critical

branches in o-glycans. Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GCNT1. The function of GCNT1 has been established by previous studies. Bierhuizen et al. (1993) provided the sequence of the developmental I antigen encoded by the cDNA for a member of a beta-1,6-N-acetylglucosaminyltransferase gene family. By Northern blot analysis, Yeh et al. (1999) showed that multiple transcripts of GCNT1 were expressed in nearly all tissues tested, whereas expression of GCNT3 (OMIM Ref. No. 606836) was more restricted. Transcripts were also readily detected in some leukemic cell lines and in colon and cervical carcinoma cell lines, but not in a lung carcinoma cell line.

[10864] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10865] Bierhuizen, M. F. A.; Mattei, M.-G.; Fukuda, M. : Expression of the developmental I antigen by a cloned human cDNA encoding a member of a beta-1,6-N-acetylglucosaminyltransferase gene family. *Genes Dev.* 7: 468-478, 1993. ; and

[10866] Pilz, A.; Woodward, K.; Povey, S.; Abbott, C. : Comparative

mapping of 50 human chromosome 9 loci in the laboratory mouse. Genomics 25: 139–149, 1995.

[10867] Further studies establishing the function and utilities of GCNT1 are found in John Hopkins OMIM database record ID 600391, and in cited publications numbered 1215 and 12157 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM_003678) is another VGAM149 host target gene. C22orf19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C22orf19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C22orf19 BINDING SITE, designated SEQ ID:9772, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10868] Another function of VGAM149 is therefore inhibition of Chromosome 22 Open Reading Frame 19 (C22orf19, Accession NM_003678). Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C22orf19.

FLJ32332 (Accession NM_144641) is another VGAM149 host target gene. FLJ32332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32332 BINDING SITE, designated SEQ ID:29466, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10869] Another function of VGAM149 is therefore inhibition of FLJ32332 (Accession NM_144641). Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ32332. FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_054016) is another VGAM149 host target gene. FUSIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUSIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUSIP1 BINDING SITE, designated SEQ ID:27622, to the nucleotide sequence of VGAM149 RNA,

herein designated VGAM RNA, also designated SEQ ID:2860.

[10870] Another function of VGAM149 is therefore inhibition of FUS Interacting Protein (serine-arginine rich) 1 (FUSIP1, Accession NM_054016). Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUSIP1. ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM_014182) is another VGAM149 host target gene. ORMDL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ORMDL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ORMDL2 BINDING SITE, designated SEQ ID:15465, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10871] Another function of VGAM149 is therefore inhibition of ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM_014182). Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ORMDL2. RAI (Accession NM_006663) is another VGAM149 host target gene. RAI

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI BINDING SITE, designated SEQ ID:13466, to the nucleotide sequence of VGAM149 RNA, herein designated VGAM RNA, also designated SEQ ID:2860.

[10872] Another function of VGAM149 is therefore inhibition of RAI (Accession NM_006663). Accordingly, utilities of VGAM149 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 150 (VGAM150) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10873] VGAM150 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM150 was detected is described hereinabove with reference to Figs. 1–8.

[10874] VGAM150 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10875] VGAM150 gene encodes a VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM150 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM150 precursor RNA is designated SEQ ID:136, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:136 is located at position 59190 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10876] VGAM150 precursor RNA folds onto itself, forming VGAM150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[10877] An enzyme complex designated DICER COMPLEX, `dices` the VGAM150 folded precursor RNA into VGAM150 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM150 RNA is designated SEQ ID:2861, and is provided hereinbelow with reference to the sequence listing part.

[10878] VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM150 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10879] VGAM150 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM150 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM150 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM150 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10880] The complementary binding of VGAM150 RNA, herein designated VGAM RNA, to host target binding sites on VGAM150 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM150 host target RNA into VGAM150 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10881] It is appreciated that VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM150 host target genes. The mRNA of each one of this plurality of VGAM150 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM150 RNA, herein designated VGAM RNA, and which when bound by VGAM150 RNA causes inhibition of translation of respective one or more VGAM150 host target proteins.

[10882] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM150 gene, herein designated VGAM GENE, on one or more VGAM150 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10883] It is yet further appreciated that a function of VGAM150 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM150 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM150 correlate with, and may be deduced from, the identity of the host target genes which VGAM150 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10884] Nucleotide sequences of the VGAM150 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM150 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM150 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM150 are further described hereinbelow with reference to Table 1.

[10885] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM150 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM150 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10886] As mentioned hereinabove with reference to Fig. 1, a function of VGAM150 gene, herein designated VGAM is inhibition of expression of VGAM150 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM150 correlate with, and may be deduced from, the identity of the target genes which VGAM150 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10887] PRO1489 (Accession NM_018584) is a VGAM150 host target gene. PRO1489 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1489, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1489 BINDING SITE, designated SEQ ID:20661, to the nucleotide sequence of VGAM150 RNA, herein designated VGAM RNA, also designated SEQ ID:2861.

[10888] A function of VGAM150 is therefore inhibition of PRO1489 (Accession NM_018584). Accordingly, utilities of VGAM150 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 151 (VGAM151) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10889] VGAM151 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM151 was detected is described hereinabove with reference to Figs. 1–8.

[10890] VGAM151 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM151 host target gene, herein designated VGAM HOST TARGET GENE,

is a human gene contained in the human genome.

[10891] VGAM151 gene encodes a VGAM151 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM151 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM151 precursor RNA is designated SEQ ID:137, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:137 is located at position 141707 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10892] VGAM151 precursor RNA folds onto itself, forming VGAM151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10893] An enzyme complex designated DICER COMPLEX, `dices` the VGAM151 folded precursor RNA into VGAM151 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM151 RNA is designated SEQ ID:2862, and is provided hereinbelow with reference to the sequence listing part.

[10894] VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM151 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10895] VGAM151 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM151 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM151 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[10896] The complementary binding of VGAM151 RNA, herein designated VGAM RNA, to host target binding sites on VGAM151 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM151 host target RNA into VGAM151 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[10897] It is appreciated that VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM151 host target genes. The mRNA of each one of this plurality of VGAM151 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM151 RNA, herein designated VGAM RNA, and which when bound by VGAM151 RNA causes inhibition of translation of respective one or more VGAM151 host target proteins.

[10898] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM151 gene, herein designated VGAM GENE, on one or more VGAM151 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[10899] It is yet further appreciated that a function of VGAM151 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM151 correlate with, and may be deduced from, the identity of the host target genes which VGAM151 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10900] Nucleotide sequences of the VGAM151 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM151 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM151 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM151 are further described hereinbelow with reference to Table 1.

[10901] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM151 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM151 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10902] As mentioned hereinabove with reference to Fig. 1, a function of VGAM151 gene, herein designated VGAM is inhibition of expression of VGAM151 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM151 correlate with, and may be deduced from, the identity of the target genes which VGAM151 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10903] PACE (Accession NM_002569) is a VGAM151 host target gene. PACE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PACE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PACE BINDING SITE, designated SEQ ID:8424, to the nucleotide sequence of VGAM151 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2862.

[10904] A function of VGAM151 is therefore inhibition of PACE (Accession NM_002569), a gene which processes pro-parathyroid hormone, pro-transforming growth factor beta. Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PACE. The function of PACE has been established by previous studies. Roebroek et al. (1986) described DNA sequences in the immediate upstream region from the FES oncogene (OMIM Ref. No. 190030). They designated this FUR (for FES upstream region) and showed that in both man and cat the sequence codes for a 4.5-kb mRNA. The nucleotide sequence of a 3.1-kb FUR-specific cDNA isolated from a human cDNA library showed an open reading frame of 1,498 bp from which the 499 carboxy-terminal amino acids of the primary FUR translation product could be deduced. Computer analysis indicated that this product, called furin, contained a possible transmembrane domain resembling that of class II MHC antigens. Roebroek et al. (1986) concluded that FUR may encode a membrane-associated protein with a recognition function. From the location of the FES gene, one can conclude that FUR is located in the region 15q25-q26. The 2

sequences are separated by less than 1.1 kb, and the direction of transcription of the 2 is the same. Studying its expression by Northern blot analysis using poly(A)-selected RNA from a variety of organs, Schalken et al. (1987) found that the FUR gene is differentially expressed, being high in organs such as liver and kidney and very low in others such as heart muscle, lung, and testis. FUR expression discriminated sharply between small cell lung cancers, which had no expression, and nonsmall cell lung cancers, which had strong elevation of expression. Hendy et al. (1995) reported experiments strongly suggesting that furin is the enzyme responsible for the physiologic processing of parathyroid hormone to PTH (OMIM Ref. No. 168450). Dubois et al. (1995) demonstrated in vitro that pro-TGFB1 (see OMIM Ref. No. 190180) was cleaved by furin to produce a biologically active TGFB1 protein. Expression of pro-TGFB1 in furin-deficient cells produced no TGFB1, while coexpression of pro-TGFB1 and furin led to processing of the precursor. Blanchette et al. (1997) showed that furin mRNA levels were increased in rat synovial cells by the addition of TGFB1. This effect was eliminated by pretreatment with actinomycin-D, suggesting to them that regulation was at

the gene transcriptional level. Treatment of rat synovio-
cytes and kidney fibroblasts with TGFB1 or TGFB2 resulted
in increased pro-TGFB1 processing, as evidenced by the
appearance of a 40-kD immunoreactive band correspond-
ing to the TGFB1 amino-terminal pro-region. Treatment
of these cells with TGFB2 resulted in a significant increase
in extracellular mature TGFB1. Blanchette et al. (1997)
concluded that TGFB1 upregulates gene expression of its
own converting enzyme.

- [10905] Full details of the abovementioned studies are described
in the following publications, the disclosure of which are
hereby incorporated by reference:
- [10906] Schalken, J. A.; Roebroek, A. J. M.; Oomen, P. P. C. A.; Wa-
genaer, S. S.; Debruyne, F. M. J.; Bloemers, H. P. J.; Van de
Ven, W. J. M. : FUR gene expression as a discriminating
marker for small cell and nonsmall cell lung carcinomas. J.
Clin. Invest. 80: 1545-1549, 1987. ; and
- [10907] Blanchette, F.; Day, R.; Dong, W.; Laprise, M.-H.; Dubois,
C. M. : TGF-beta-1 regulates gene expression of its own
converting enzyme furin. J. Clin. Invest. 99: 1974-1983,
1997.
- [10908] Further studies establishing the function and utilities of
PACE are found in John Hopkins OMIM database record ID

136950, and in cited publications numbered 3576–3583 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ13241

(Accession NM_025088) is another VGAM151 host target gene. FLJ13241 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ13241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13241 BINDING SITE, designated SEQ ID:24707, to the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, also designated SEQ ID:2862.

[10909] Another function of VGAM151 is therefore inhibition of FLJ13241 (Accession NM_025088). Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13241. KIAA0546 (Accession XM_049055) is another VGAM151 host target gene. KIAA0546 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0546 BINDING SITE, designated SEQ ID:35331, to the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, also designated SEQ ID:2862.

[10910] Another function of VGAM151 is therefore inhibition of KIAA0546 (Accession XM_049055). Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0546. KIAA1449 (Accession NM_020839) is another VGAM151 host target gene. KIAA1449 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1449, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1449 BINDING SITE, designated SEQ ID:21898, to the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, also designated SEQ ID:2862.

[10911] Another function of VGAM151 is therefore inhibition of KIAA1449 (Accession NM_020839). Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1449. LOC113523 (Accession XM_054378) is another

VGAM151 host target gene. LOC113523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113523 BINDING SITE, designated SEQ ID:36151, to the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, also designated SEQ ID:2862.

[10912] Another function of VGAM151 is therefore inhibition of LOC113523 (Accession XM_054378). Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113523. LOC133584 (Accession XM_059661) is another VGAM151 host target gene. LOC133584 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC133584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133584 BINDING SITE, designated SEQ ID:37045, to the nucleotide sequence of VGAM151 RNA, herein designated VGAM RNA, also designated SEQ ID:2862.

[10913] Another function of VGAM151 is therefore inhibition of LOC133584 (Accession XM_059661). Accordingly, utilities of VGAM151 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133584. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 152 (VGAM152) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[10914] VGAM152 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM152 was detected is described hereinabove with reference to Figs. 1–8.

[10915] VGAM152 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[10916] VGAM152 gene encodes a VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM152

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM152 precursor RNA is designated SEQ ID:138, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:138 is located at position 36222 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[10917] VGAM152 precursor RNA folds onto itself, forming VGAM152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[10918] An enzyme complex designated DICER COMPLEX, `dices` the VGAM152 folded precursor RNA into VGAM152 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM152 RNA is designated SEQ ID:2863, and is provided hereinbelow with reference to the sequence listing part.

[10919] VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM152 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[10920] VGAM152 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM152 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM152 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[10921] The complementary binding of VGAM152 RNA, herein designated VGAM RNA, to host target binding sites on VGAM152 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM152 host target RNA into VGAM152 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[10922] It is appreciated that VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM152 host target genes. The mRNA of

each one of this plurality of VGAM152 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM152 RNA, herein designated VGAM RNA, and which when bound by VGAM152 RNA causes inhibition of translation of respective one or more VGAM152 host target proteins.

[10923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM152 gene, herein designated VGAM GENE, on one or more VGAM152 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[10924] It is yet further appreciated that a function of VGAM152 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM152 correlate with, and may be deduced from, the identity of the host target genes which VGAM152 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[10925] Nucleotide sequences of the VGAM152 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM152 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM152 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM152 are further described hereinbelow with reference to Table 1.

[10926] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM152 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM152 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[10927] As mentioned hereinabove with reference to Fig. 1, a function of VGAM152 gene, herein designated VGAM is inhibition of expression of VGAM152 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM152 correlate with, and may be deduced from, the identity of the target genes which VGAM152 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[10928] Apical Protein-like (*Xenopus laevis*) (APXL, Accession NM_001649) is a VGAM152 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7354, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10929] A function of VGAM152 is therefore inhibition of Apical Protein-like (*Xenopus laevis*) (APXL, Accession

NM_001649), a gene which is implicated in amiloride-sensitive sodium channel activity. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL has been established by previous studies. APXL is a human homolog of the *Xenopus laevis* APX gene which is implicated in amiloride-sensitive sodium channel activity (Schiaffino et al., 1995). The gene contains 10 exons and spans approximately 160 kb of Xp22.3 in the ocular albinism type 1 (OA1; 300500) critical region. The full-length mRNA is approximately 7.5 kb, and Schiaffino et al. (1995) isolated several clones from a retinal cDNA library that corresponded to this mRNA. The authors found that, along with retina, the gene is expressed in melanoma cells, brain, placenta, lung, kidney, and pancreas. The protein is 1,616 amino acids in length. APXL was deleted in 2 patients with contiguous gene syndromes including OA1 and in 1 patient with isolated OA1. Comparative mapping of the X chromosome in eutherian mammals has revealed distinct regions of conservation as well as evolutionary rearrangements between human and mouse. Dinulos et al. (1996) mapped the murine homologs of OA1 and APXL. They found that the 2 genes

map to bands F2–F3 in both *M. spretus* and the laboratory strains C57BL/6J, defining a new rearrangement between human and mouse X chromosomes.

[10930] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10931] Dinulos, M. B.; Bassi, M. T.; Rugarli, E. I.; Chapman, V.; Ballabio, A.; Disteche, C. M. : A new region of conservation is defined between human and mouse X chromosomes. *Genomics* 35: 244–247, 1996. ; and

[10932] Schiaffino, M. V.; Bassi, M. T.; Rugarli, E. I.; Renieri, A.; Galli, L.; Ballabio, A. : Cloning of a human homologue of the *Xenopus laevis* APX gene from the ocular albinism type 1 criti.

[10933] Further studies establishing the function and utilities of APXL are found in John Hopkins OMIM database record ID 300103, and in cited publications numbered 8797–8798 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678) is another VGAM152 host target gene. ATP1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

ATP1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B2 BINDING SITE, designated SEQ ID:7392, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10934] Another function of VGAM152 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678), a gene which catalyzes the hydrolysis of ATP coupled with the exchange of Na⁺/K⁺ ions across the plasma membrane. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B2. The function of ATP1B2 has been established by previous studies. In the mouse, Malo et al. (1990) mapped the beta-2 subunit of sodium-potassium-ATPase to chromosome 11 in a segment that is conserved on the pericentromeric region of human chromosome 17. Thus, Malo et al. (1990) speculated that the human ATP1B2 gene is on the proximal short arm or pericentric area of chromosome 17. By somatic cell hybrid analysis, Hsieh et al. (1990) demonstrated that the gene is

indeed located on human chromosome 17 and confirmed the assignment to mouse chromosome 11, They referred to the gene as AMOG (adhesion molecule on glia). The adhesion molecule on glia is an integral membrane glycoprotein of MW 45–50 K that is expressed by glial cells and mediates granule neuron migration along Bergmann glial cells in the developing cerebellum. The cDNA sequence of the mouse gene (Pagliusi et al., 1989) shows structural similarity to the beta subunit of Na,K-ATPase (ATP1B1; 182330). This enzyme consists of 2 subunits: a catalytic alpha subunit and a beta subunit of unknown function. Like ATP1B1, AMOG is molecularly associated with the alpha subunit and influences its catalytic activity. AMOG may be the same as what is referred to here as ATP1B2. Another beta-isoform gene expressed primarily in brain was isolated by Martin-Vasallo et al. (1989); its sequence is 97% identical to that for AMOG (Gloor et al., 1990). By study of recombinant inbred strains, Hsieh et al. (1990) placed the Amog locus close to the genes for zinc finger protein-3 (OMIM Ref. No. 194480) and the asialoglycoprotein receptor (108360, 108361) in a region of mouse chromosome 11 that is homologous to human 17p.

[10935] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [10936] Gloor, S.; Antonicek, H.; Sweadner, K. J.; Pagliusi, S.; Frank, R.; Moos, M.; Schachner, M. : The adhesion molecule on glia (AMOG) is a homologue of the beta subunit of the Na,K-ATPase. J. Cell Biol. 110: 165-174, 1990. ; and
- [10937] Martin-Vasallo, P.; Dackowski, P.; Emanuel, J. R.; Levenson, R. : Identification of a putative isoform of the Na,K-ATPase beta subunit: primary structure and tissue-specific expression.
- [10938] Further studies establishing the function and utilities of ATP1B2 are found in John Hopkins OMIM database record ID 182331, and in cited publications numbered 12450-12454 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093) is another VGAM152 host target gene. CBFA2T2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBFA2T2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE, designated SEQ ID:11548, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10939] Another function of VGAM152 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 has been established by previous studies. To identify potential new genes homologous to ETO (OMIM Ref. No. 133435), Fracchiolla et al. (1998) screened the EST database using the entire ETO cDNA sequence as a probe. Among the ESTs identified, they selected 2 overlapping clones and sequenced them to completion. A putative translation initiation site was identified by the presence of a strong Kozak consensus sequence, followed by a 1,725-bp open reading frame coding for a putative protein of 575 amino acids. They named this gene EHT for 'ETO homolog on chromosome twenty.' The putative EHT protein is approximately 65% identical to ETO/MTG8 (OMIM Ref. No. 133435) and ap-

proximately 24% identical to an ETO *Drosophila* homolog, Nervy. Kitabayashi et al. (1998) reported the cloning of a similar cDNA, which they named MTGR1 (myeloid translocation gene-related protein-1). Their data suggested the presence of 2 alternative 5-prime ends of the MTGR1/EHT gene. Cytogenetic studies had shown that the 20q11 region is deleted in approximately 10% of cases of polycythemia vera, approximately 5% of cases of myelodysplastic syndromes, and approximately 3% of cases of acute myeloid leukemias. Kitabayashi et al. (1998) showed the direct interaction of MTGR1 in the AML1-MTG8 fusion protein, leading to an enhancement of cell proliferation mediated by granulocyte colony-stimulating factor (CSF3; 138970) in a murine myeloid model. This suggested that MTGR1 has an oncogenic rather than a tumor suppressor activity. Nevertheless, when MTGR1 was transfected alone into the same murine myeloid model cell line, the proliferative response to CSF was lower than that in the normal control, thus suggesting a possible negative growth control in normal cells.

[10940] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [10941] Fracchiolla, N. S.; Colombo, G.; Finelli, P.; Maiolo, A. T.; Neri, A. : EHT, a new member of the MTG8/ETO gene family, maps on 20q11 region and is deleted in acute myeloid leukemias. (Letter) Blood 92: 3481–3484, 1998. ; and
- [10942] Kitabayashi, I.; Ida, K.; Morohoshi, F.; Yokoyama, A.; Mitsuhashi, N.; Shimizu, K.; Nomura, N.; Hayashi, Y.; Ohki, M. : The AML1–MTG8 leukemic fusion protein forms a complex with a novel.
- [10943] Further studies establishing the function and utilities of CBFA2T2 are found in John Hopkins OMIM database record ID 603672, and in cited publications numbered 344 and 8659–8660 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cartilage Associated Protein (CRTAP, Accession NM_006371) is another VGAM152 host target gene. CRTAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CRTAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CRTAP BINDING SITE, designated SEQ ID:13061, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ

ID:2863.

[10944] Another function of VGAM152 is therefore inhibition of Cartilage Associated Protein (CRTAP, Accession NM_006371), a gene which is a novel developmentally regulated chick embryo protein. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CRTAP. The function of CRTAP has been established by previous studies. Castagnola et al. (1997) isolated a mouse *Crtap* cDNA from a subtracted library specific for mRNAs highly expressed in hypertrophic chondrocytes compared to proliferating and early differentiating chondrocytes. Using a mouse *Crtap* clone to screen a human fetal brain cDNA library, Tonachini et al. (1999) identified human CRTAP cDNA clones. Human CRTAP encodes a deduced 401-amino acid protein with a putative signal peptide of 26 amino acids. CRTAP contains 2 potential N-glycosylation signals. CRTAP shares 89% amino acid sequence identity with mouse *Crtap* and 51% identity with the chick homolog. The mouse and human genes contain a C-terminal region of approximately 120 amino acids not present in the chick protein. Using Northern blot analysis of human tissues, Tonachini et al. (1999) detected 2-kb

and 4-kb CRTAP transcripts in brain, heart, kidney, lung, small intestine, and skeletal muscle. In all tissues except brain, the 2-kb transcript was more abundant. Using immunohistochemistry, the authors detected CRTAP expression in articular chondrocytes. In mouse, Morello et al. (1999) detected 3 *Crtap* transcripts in a range of tissues, including all mouse embryonic cartilages. In chick, Castagnola et al. (1997) detected a single *Crtap* transcript in a broad range of embryonic tissues with the strongest expression in the developing cartilage. They detected expression in the extracellular matrix of the forming cartilage surrounding the notochord, the developing sclera, the sphenoid and mandibular cartilage, the long bone cartilage, and the developing sternal cartilage

[10945] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10946] Castagnola, P.; Gennari, M.; Morello, R.; Tonachini, L.; Marin, O.; Gaggero, A.; Cancedda, R. : Cartilage associated protein (CASP) is a novel developmentally regulated chick embryo protein. *J. Cell Sci.* 110: 1351–1359, 1997. ; and

[10947] Morello, R.; Tonachini, L.; Monticone, M.; Viggiano, L.; Rocchi, M.; Cancedda, R.; Castagnola, P. : cDNA cloning,

characterization and chromosome mapping of Crtap encoding the mouse carti.

[10948] Further studies establishing the function and utilities of CRTAP are found in John Hopkins OMIM database record ID 605497, and in cited publications numbered 6396–6398 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199) is another VGAM152 host target gene. EIF2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C1 BINDING SITE, designated SEQ ID:14499, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10949] Another function of VGAM152 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199), a gene which plays an important role in the eukaryotic peptide chain initiation process. Accordingly, utilities of VGAM152 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with EIF2C1. The function of EIF2C1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM118. Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 3 (GNB3, Accession NM_002075) is another VGAM152 host target gene. GNB3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GNB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GNB3 BINDING SITE, designated SEQ ID:7853, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10950] Another function of VGAM152 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Beta Polypeptide 3 (GNB3, Accession NM_002075), a gene which transduces signals from G protein-coupled receptors to intracellular effectors. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNB3. The function of GNB3 has been established by previous stud-

ies. Levine et al. (1990) cloned a third form of the G protein beta-subunit polypeptide distinct from the 36-kD form (GNB1; 139380) and the 35-kD form (GNB2; 139390). The GNB3 cDNA corresponded to a 2.0-kb mRNA expressed in all tissues and clonal cell lines examined. The encoded peptide consisted of 340 amino acid residues. Modi et al. (1989) mapped the GNB3 gene to 12p13 by use of somatic cell hybrids and in situ hybridization. Levine et al. (1990) mapped the gene to 12pter-p12.3 by Southern analysis of somatic cell hybrids and by in situ hybridization. Siffert et al. (1995) and Pietruck et al. (1996) demonstrated an enhanced signal transduction via pertussis toxin-sensitive G proteins in lymphoblasts and fibroblasts from selected patients with essential hypertension. They speculated that structural changes in the alpha, beta, or gamma subunit of heterotrimeric G proteins could be responsible for the enhanced G-protein reactivity in hypertensive cells. In studies of the GNB3 gene, they demonstrated an 825C-T polymorphism. Although the polymorphism did not affect the amino acid sequence of the beta-3 subunit, the T allele was associated with deletion of nucleotides 498-620 of exon 9 (139130.0001). This was found to be an example

of alternative splicing caused by a nucleotide change outside the splice donor and acceptor sites. Other examples include the alternative splicing of the platelet membrane glycoprotein IIIa, as reported by Jin et al. (1996), in Glanzmann thrombasthenia (OMIM Ref. No. 273800), in the human growth hormone receptor (OMIM Ref. No. 600946) by Stallings-Mann et al. (1996), and in the fibrillin-1 gene (OMIM Ref. No. 134797) in Marfan syndrome by Liu et al. (1997).

[10951] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10952] Levine, M. A.; Modi, W. S.; O'Brien, S. J. : Chromosomal localization of the genes encoding two forms of the G-protein beta polypeptide, beta-1 and beta-3, in man. *Genomics* 8: 380-386, 1990. ; and

[10953] Siffert, W.; Roszkopf, D.; Moritz, A.; Wieland, T.; Kaldenberg-Stasch, S.; Kettler, N.; Hartung, K.; Beckmann, S.; Jakobs, K. H. : Enhanced G protein activation in immortalized lymphobl.

[10954] Further studies establishing the function and utilities of GNB3 are found in John Hopkins OMIM database record ID 139130, and in cited publications numbered 471 and

4715–4727 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 5–hydroxytryptamine (serotonin) Receptor 1D (HTR1D, Accession NM_000864) is another VGAM152 host target gene. HTR1D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTR1D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR1D BINDING SITE, designated SEQ ID:6529, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10955] Another function of VGAM152 is therefore inhibition of 5–hydroxytryptamine (serotonin) Receptor 1D (HTR1D, Accession NM_000864), a gene which belongs to G-protein coupled receptor. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR1D. The function of HTR1D has been established by previous studies. The serotonin 1D receptor was initially characterized by radioligand binding procedures using membranes derived from bovine caudate nucleus. The 5-HT-1D re-

ceptor is known to be a G protein–coupled receptor. Sumatriptan, an agent effective in the treatment of acute migraine, is the only ligand yet identified that is selective for the 5–HT–1D receptor. Weinshank et al. (1992) reported the cloning, deduced amino acid sequences, pharmacologic properties, and second–messenger coupling of a pair of human 5–HT–1D receptor genes, which they designated alpha and beta due to their strong similarities. Both genes have no introns in their coding regions, are expressed in the human cerebral cortex, and can couple to inhibition of adenylate cyclase activity. Their pharmacologic binding properties match closely those of human, bovine, and guinea pig 5–HT–1D sites. Libert et al. (1991) obtained cDNA clones encoding 4 receptors of the G protein–coupled receptor family by selective amplification and cloning from thyroid cDNA. One of these clones, termed RDC4 by them, showed close structural similarity with the serotonin 5HT1A receptor (OMIM Ref. No. 109760). By in situ hybridization, they demonstrated that the gene (HTR1D) is located on chromosome 1 at 1p36.3–p34.3. By Southern blot analysis of a hybrid cell panel, Jin et al. (1992) showed that the HTR1D gene is located on chromosome 1. Wilkie et al. (1993) showed that

the homologous gene in the mouse is located on chromosome 4.

[10956] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10957] Weinshank, R. L.; Zgombick, J. M.; Macchi, M. J.; Branchek, T. A.; Hartig, P. R. : Human serotonin 1D receptor is encoded by a subfamily of two distinct genes: 5-HT(1D-alpha) and 5-HT(1D-beta). Proc. Nat. Acad. Sci. 89: 3630-3634, 1992. ; and

[10958] Wilkie, T. M.; Chen, Y.; Gilbert, D. J.; Moore, K. J.; Yu, L.; Simon, M. I.; Copeland, N. G.; Jenkins, N. A. : Identification, chromosomal location, and genome organization of mammalian.

[10959] Further studies establishing the function and utilities of HTR1D are found in John Hopkins OMIM database record ID 182133, and in cited publications numbered 10613, 1061 and 11892 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Insulin-like Growth Factor 1 Receptor (IGF1R, Accession NM_000875) is another VGAM152 host target gene. IGF1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGF1R,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF1R BINDING SITE, designated SEQ ID:6556, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10960] Another function of VGAM152 is therefore inhibition of Insulin-like Growth Factor 1 Receptor (IGF1R, Accession NM_000875), a gene which binds insulin-like growth factors and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF1R. The function of IGF1R has been established by previous studies. Flier et al. (1986) studied a monoclonal antibody to the receptor for type I insulin-like growth factor (IGF1; 147440). This might be the site of the change in some forms of growth disturbance. Ullrich et al. (1986) determined the complete primary structure of the receptor for IGF I from cloned cDNA. The deduced sequence predicts a 1,367-amino acid receptor precursor, including a 30-residue signal peptide, which is removed during translocation of the nascent polypeptide chain. Cleavage of the precursor generates alpha and beta sub-

units as in the case of the insulin receptor (INSR; 147670). Abbott et al. (1992) determined that the IGF1R gene contains 21 exons and spans about 100 kb. Cooke et al. (1991) analyzed the promoter region and found that the 5-prime flanking and untranslated region is GC-rich and contains numerous potential SP1 and AP2 binding sites as well as a thyroid response element, but no TATA or CCAAT elements. Prager et al. (1992) showed that a mutant human IGF-I receptor interfered with the expected suppression of growth hormone in cultured rat pituitary cells, thus demonstrating a dominant-negative phenotype. (The 'dominant-negative' concept was first clearly articulated by Herskowitz (1987). He recognized 2 classes. The first class comprises multimeric proteins dependent on oligomerization for activity; the presence in a multimer of a mutant subunit with intact binding but altered catalytic domains can abrogate the function of the entire multimer. The second class involves monomeric proteins, in which dominant-negative mutations can occur if substrate is limiting; a mutant able to bind the substrate but not metabolize it would have this effect.) Using a yeast 2-hybrid system, Dey et al. (1998) identified a regulatory subunit of phosphatidylinositol (PI) 3-kinase, PIK3R3

(OMIM Ref. No. 606076), as a binding partner of IGF1R. They concluded that the SH2 domain of PIK3R3 interacts with IGF1R and INSR in a kinase-dependent manner, providing an alternative pathway for the activation of PI 3-kinase by these 2 receptors. Rotem-Yehudar et al. (2001) found evidence that IGF1R associated with SNAP29 (OMIM Ref. No. 604202), a synaptosomal-associated protein, and with EHD1 (OMIM Ref. No. 605888), a protein containing motifs important for protein-protein interaction and for intracellular sorting. Through immunoprecipitation of rat tissues, they found that SNAP29 and EHD1 are present in complexes with IGF1R. They also found that IGF1 induction of EHD1-transfected CHO cells results in intracellular colocalization of EHD1 and IGF1R. Animal model experiments lend further support to the function of IGF1R. Fernandez et al. (2001) developed transgenic mice overexpressing a dominant-negative IGF1R, containing a mutation that abolishes ATPase activity, specifically targeted to skeletal muscle. They found that mutant IGF1R impairs the function of both the normal endogenous IGF1R and the insulin receptor, and that mice overexpressing the mutant IGF1R developed insulin resistance and pancreatic beta-cell dysfunction followed by diabetes.

By coimmunoprecipitation experiments, Fernandez et al. (2001) showed interaction between mutant and normal IGF1R hemireceptors as well as between mutant IGF1R and INSR, suggesting the formation of nonfunctional hybrid receptors. Through biochemical analysis, they showed that the mutant hemireceptor fails to autophosphorylate and thereby abrogates the normal function of the hybrid receptors. To identify genetic determinants of hypoxic cell death, Scott et al. (2002) screened for hypoxia-resistant mutants in *C. elegans* and found that specific reduction-of-function mutants of *daf2*, an insulin/insulin-like growth factor receptor homolog gene, were profoundly hypoxia resistant. The hypoxia resistance was acutely inducible just before hypoxic exposure and was mediated through the AKT1/PDK1/forkhead transcription factor pathway overlapping with but distinct from signaling pathways regulating lifespan and stress resistance. Selective neuronal and muscle expression of *daf2* wildtype restored hypoxic death, and *daf2* reduction of function mutants prevented hypoxia-induced muscle and neuronal cell death, demonstrating a potential for insulin/insulin-like growth factor receptor modulation in prophylaxis against hypoxic injury of neurons and myocytes.

- [10961] It is appreciated that the abovementioned animal model for IGF1R is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.
- [10962] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [10963] Fernandez, A. M.; Kim, J. K.; Yakar, S.; Dupont, J.; Hernandez-Sanchez, C.; Castle, A. L.; Filmore, J.; Shulman, G. I.; Le Roith, D. : Functional inactivation of the IGF-I and insulin receptors in skeletal muscle causes type 2 diabetes. *Genes Dev.* 15: 1926-1934, 2001. ; and
- [10964] All-Ericsson, C.; Girnita, L.; Seregard, S.; Bartolazzi, A.; Jager, M. J.; Larsson, O. : Insulin-like growth factor-1 receptor in uveal melanoma: a predictor for metastatic disease and.
- [10965] Further studies establishing the function and utilities of IGF1R are found in John Hopkins OMIM database record ID 147370, and in cited publications numbered 11275-11286, 5228, 11287-11288, 11235, 1128 and 11323-11327 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Intermediate/small Conductance Calcium-

activated Channel, Subfamily N, Member 4 (KCNN4, Accession NM_002250) is another VGAM152 host target gene. KCNN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNN4 BINDING SITE, designated SEQ ID:8036, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10966] Another function of VGAM152 is therefore inhibition of Potassium Intermediate/small Conductance Calcium-activated Channel, Subfamily N, Member 4 (KCNN4, Accession NM_002250), a gene which forms a voltage-independent potassium channel that is activated by intracellular calcium. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNN4. The function of KCNN4 has been established by previous studies. The calcium-activated potassium channels (KCa channels) have been classified into 3 groups. Large conductance (BK) channels are gated by the concerted actions of internal

calcium ions and membrane potential and have a unit conductance of 100 to 220 picoSiemens (pS). Intermediate conductance (IK) and small conductance (SK) channels are gated solely by internal calcium ions, with a unit conductance of 20 to 85 pS and 2 to 20 pS, respectively, and are more sensitive to calcium than are BK channels. Each type of channel shows a distinct pharmacology (Ishii et al., 1997). Joiner et al. (1997) cloned cDNAs encoding KCNN4, which they called SK4. The predicted 427-amino acid sequence of KCNN4 was approximately 40% identical to that of the rat and human SK channel proteins rSK1, rSK2, rSK3 and hSK1. Sequence analysis revealed that, like the SK channel proteins, KCNN4 contained 6 putative transmembrane domains, a conserved pore region, and a leucine zipper-like motif near the C terminus. When expressed in Chinese hamster ovary cells, KCNN4 generated a conductance of approximately 12 pS and had a very high affinity for calcium. By Northern analysis, the authors found that KCNN4 was expressed as 2.6-kb and 3.8-kb transcripts in placenta and at lower levels in lung and pancreas. On the basis of its expression pattern, physiologic properties, and low homology to other SK channel proteins, Joiner et al. (1997) proposed that KCNN4 belongs to a new sub-

family of SK channels.

[10967] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10968] Ghanshani, S.; Coleman, M.; Gustavsson, P.; Wu, A. C.-L.; Gargus, J. J.; Gutman, G. A.; Dahl, N.; Mohrenweiser, H.; Chandy, K. G. : Human calcium-activated potassium channel gene KCNN4 maps to chromosome 19q13.2 in the region deleted in Diamond-Blackfan anemia. *Genomics* 51: 160-161, 1998. ; and

[10969] Ishii, T. M.; Silvia, C.; Hirschberg, B.; Bond, C. T.; Adelman, J. P.; Maylie, J. : A human intermediate conductance calcium-activated potassium channel. *Proc. Nat. Acad. Sci.* 94: 11651-.

[10970] Further studies establishing the function and utilities of KCNN4 are found in John Hopkins OMIM database record ID 602754, and in cited publications numbered 5883-5886 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM_139012) is another VGAM152 host target gene. MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3 are HOST TARGET binding sites found in untrans-

lated regions of mRNA encoded by MAPK14, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK14 BINDING SITE1 through MAPK14 BINDING SITE3, designated SEQ ID:29106, SEQ ID:29113 and SEQ ID:7002 respectively, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10971] Another function of VGAM152 is therefore inhibition of Mitogen-activated Protein Kinase 14 (MAPK14, Accession NM_139012), a gene which is important for cytokine production; responds to changes in extracellular osmolarity. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK14. The function of MAPK14 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107.P23 (Accession NM_006601) is another VGAM152 host target gene. P23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P23, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P23 BINDING SITE, designated SEQ ID:13380, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10972] Another function of VGAM152 is therefore inhibition of P23 (Accession NM_006601), a gene which is a component of unstimulated progesterone receptor complex. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P23. The function of P23 has been established by previous studies. P23 was first observed as a component of the unactivated avian progesterone receptor complex, along with HSP70 (see OMIM Ref. No. 140550) and HSP90 (see OMIM Ref. No. 140571) (Smith et al., 1990). Using the chicken p23 sequence as probe, Johnson et al. (1994) cloned P23 from a human testis cDNA library. The deduced 160-amino acid protein has a calculated molecular mass of about 19 kD and contains several putative phosphorylation sites. P23 shares about 96% sequence identity with the chicken homolog. Western blot analysis revealed a 23-kD band in tissue and cell lysates from several mammalian species including human.

Freeman and Yamamoto (2002) determined that the P23 molecular chaperone localizes to genomic response elements in a hormone-dependent manner and showed that it could disrupt receptor-mediated transcriptional activation.

[10973] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10974] Johnson, J. L.; Beito, T. G.; Krco, C. J.; Toft, D. O. : Characterization of a novel 23-kilodalton protein of unactive progesterone receptor complexes. *Molec. Cell. Biol.* 14: 1956-1963, 1994. ; and

[10975] Freeman, B. C.; Yamamoto, K. R. : Disassembly of transcriptional regulatory complexes by molecular chaperones. *Science* 296: 2232-2235, 2002.

[10976] Further studies establishing the function and utilities of P23 are found in John Hopkins OMIM database record ID 607061, and in cited publications numbered 5402-5404 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_012231) is another VGAM152 host target gene. PRDM2 BINDING SITE1 and PRDM2 BINDING SITE2 are

HOST TARGET binding sites found in untranslated regions of mRNA encoded by PRDM2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE1 and PRDM2 BINDING SITE2, designated SEQ ID:14534 and SEQ ID:18001 respectively, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10977] Another function of VGAM152 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_012231), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Serine Hydroxymethyltransferase 2 (mitochondrial) (SHMT2, Accession NM_005412) is another VGAM152 host target gene. SHMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SHMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHMT2 BINDING SITE, designated SEQ ID:11879, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10978] Another function of VGAM152 is therefore inhibition of Serine Hydroxymethyltransferase 2 (mitochondrial) (SHMT2, Accession NM_005412), a gene which interconverts serine and glycine. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHMT2. The function of SHMT2 has been established by previous studies. By human-hamster hybrids, Kao et al. (1969) have demonstrated that the human complement for hamster glycine(-)A auxotroph is located on chromosome 12. The enzyme, presence of which in human cells complements the deficiency in hamster cells, is thought to be serine hydroxymethyltransferase. Law and Kao (1978) summarized data suggesting the order 12pter--TPI--GAPD--SHMT on chromosome 12. SHMT lies on the proximal part of 12q between the centromere and Pep-B. The regional localiza-

tion is 12q12–q14. Garrow et al. (1993) cloned human cDNAs for both the cytosolic and the mitochondrial SHMT isozymes by functional complementation of an *Escherichia coli* glyA mutant with a human cDNA library. By fluorescence in situ hybridization, they demonstrated that the cytosolic (SHMT1; 182144) and mitochondrial (SHMT2) genes localized to 17p11.2 and 12q13, respectively. The high degree of nucleotide sequence identity between the 2 isozymes, as well as the presence of keratin genes in both chromosomal regions, was considered to be consistent with the occurrence of a duplication event in the origin of these regions of chromosomes 12 and 17. Stover et al. (1997) found that the SHMT2 gene, called mSHMT by them, is composed of 11 exons and spans approximately 4.5 kb. Amino acids 1 to 29 encode a mitochondrial import presequence; the corresponding mRNA contains 2 potential ATG start sites, which are encoded by separate exons. Translation initiation from the first ATG is not essential for SHMT2 activity and import into the mitochondria.

[10979] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [10980] Law, M. L.; Kao, F.-T. : Induced segregation of human syntenic genes by 5-bromodeoxyuridine plus near-visible light. *Somat. Cell Genet.* 4: 465-476, 1978. ; and
- [10981] Stover, P. J.; Chen, L. H.; Suh, J. R.; Stover, D. M.; Key-omarsi, K.; Shane, B. : Molecular cloning, characterization, and regulation of the human mitochondrial serine hydroxymethyltransfer.
- [10982] Further studies establishing the function and utilities of SHMT2 are found in John Hopkins OMIM database record ID 138450, and in cited publications numbered 4810-481 and 4969 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 35 (CMP-sialic acid transporter), Member 1 (SLC35A1, Accession NM_006416) is another VGAM152 host target gene. SLC35A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC35A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC35A1 BINDING SITE, designated SEQ ID:13126, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10983] Another function of VGAM152 is therefore inhibition of Solute Carrier Family 35 (CMP–sialic acid transporter), Member 1 (SLC35A1, Accession NM_006416), a gene which transports cmp–sialic acid from the cytosol into golgi vesicles. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC35A1. The function of SLC35A1 has been established by previous studies. By searching an EST database, followed by 5–prime RACE on an adult liver cDNA pool, Ishida et al. (1996) obtained a cDNA encoding SLC35A1, the human homolog of the murine cytidine monophosphate (CMP)–sialic acid transporter. The deduced 337–amino acid protein is approximately 65% identical to SLC35A2 (OMIM Ref. No. 314375). Ishida et al. (1998) used wheat germ agglutination sensitivity assays and flow cytometry analysis to show that SLC35A1 corrects the sialic acid transport deficiency in a mutant cell line. Immunoblot analysis showed that SLC35A1 is expressed as an approximately 29–kD protein in microsomal vesicles. Immunofluorescence microscopy demonstrated expression in the Golgi region, with the C terminus exposed to the cytosol. Northern blot analysis revealed ubiquitous expression of a 2.0–kb transcript.

[10984] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10985] Ishida, N.; Ito, M.; Yoshioka, S.; Sun-Wada, G.-H.; Kawakita, M. : Functional expression of human Golgi CMP-sialic acid transporter in the Golgi complex of a transporter-deficient Chinese hamster ovary cell mutant. J. Biochem. 124: 171-178, 1998. ; and

[10986] Ishida, N.; Miura, N.; Yoshioka, S.; Kawakita, M. : Molecular cloning and characterization of a novel isoform of the human UDP-galactose transporter, and of related complementary DNAs be.

[10987] Further studies establishing the function and utilities of SLC35A1 are found in John Hopkins OMIM database record ID 605634, and in cited publications numbered 450 and 8228 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM_139071) is another VGAM152 host target gene. SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCD1, cor-

responding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2, designated SEQ ID:29145 and SEQ ID:9047 respectively, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10988] Another function of VGAM152 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM_139071), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD1. The function of SMARCD1 has been established by previous studies. Chromatin is actively remodeled during development. Chromatin remodeling of certain genes appears to precede their transcriptional activation. In yeast, the multisubunit SWI/SNF complex is thought to be responsible for chromatin remodeling. Wang et al. (1996) isolated an analogous SWI/SNF complex from the human YT cell line. They found that the resultant complexes are composed of 9 to 12 polypeptides,

which they termed BAFs (for BRG1-associated factors).

Wang et al. (1996) isolated the BAF60a subunit, which encodes a polypeptide of 435 amino acids and is homologous to the yeast SWP73 gene. The authors used BAF60a as a probe to isolate 2 closely related homologs, BAF60b (OMIM Ref. No. 601736) and BAF60c (OMIM Ref. No. 601737). By PCR of a somatic cell hybrid panel and radiation hybrid analysis, Ring et al. (1998) mapped the SMARCD1 gene to chromosome 12q13-q14.

[10989] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[10990] Ring, H. Z.; Vameghi-Meyers, V.; Wang, W.; Crabtree, G. R.; Francke, U. : Five SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin (SMARC) genes are dispersed in the human genome. *Genomics* 51: 140-143, 1998. ; and

[10991] Wang, W.; Xue, Y.; Zhou, S.; Kuo, A.; Cairns, B. R.; Crabtree, G. R. : Diversity and specialization of mammalian SWI/SNF complexes. *Genes Dev.* 10: 2117-2130, 1996.

[10992] Further studies establishing the function and utilities of SMARCD1 are found in John Hopkins OMIM database record ID 601735, and in cited publications numbered

9322–9323 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434J193 (Accession XM_048452) is another VGAM152 host target gene. DKFZP434J193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434J193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434J193 BINDING SITE, designated SEQ ID:35162, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10993] Another function of VGAM152 is therefore inhibition of DKFZP434J193 (Accession XM_048452). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434J193. DKFZP564M182 (Accession XM_085525) is another VGAM152 host target gene. DKFZP564M182 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP564M182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of DKFZP564M182 BINDING SITE, designated SEQ ID:38220, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10994] Another function of VGAM152 is therefore inhibition of DKFZP564M182 (Accession XM_085525). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564M182. FLJ10290 (Accession NM_018047) is another VGAM152 host target gene. FLJ10290 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10290 BINDING SITE, designated SEQ ID:19797, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10995] Another function of VGAM152 is therefore inhibition of FLJ10290 (Accession NM_018047). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10290. FLJ13194 (Accession NM_025146) is another VGAM152

host target gene. FLJ13194 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13194 BINDING SITE, designated SEQ ID:24787, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10996] Another function of VGAM152 is therefore inhibition of FLJ13194 (Accession NM_025146). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13194. FLJ21870 (Accession NM_023016) is another VGAM152 host target gene. FLJ21870 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21870 BINDING SITE, designated SEQ ID:23279, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10997] Another function of VGAM152 is therefore inhibition of FLJ21870 (Accession NM_023016). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21870. H_GS165L15.1 (Accession NM_004904) is another VGAM152 host target gene. H_GS165L15.1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by H_GS165L15.1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H_GS165L15.1 BINDING SITE, designated SEQ ID:11338, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10998] Another function of VGAM152 is therefore inhibition of H_GS165L15.1 (Accession NM_004904). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H_GS165L15.1. KIAA0295 (Accession XM_042833) is another VGAM152 host target gene. KIAA0295 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0295, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0295 BINDING SITE, designated SEQ ID:33780, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[10999] Another function of VGAM152 is therefore inhibition of KIAA0295 (Accession XM_042833). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0295. KIAA0356 (Accession XM_038655) is another VGAM152 host target gene. KIAA0356 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0356, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0356 BINDING SITE, designated SEQ ID:32893, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11000] Another function of VGAM152 is therefore inhibition of KIAA0356 (Accession XM_038655). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0356. KIAA0853 (Accession NM_015070) is another VGAM152 host target gene. KIAA0853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0853 BINDING SITE, designated SEQ ID:17440, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11001] Another function of VGAM152 is therefore inhibition of KIAA0853 (Accession NM_015070). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0853. KIAA1102 (Accession XM_044461) is another VGAM152 host target gene. KIAA1102 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1102 BINDING SITE, designated SEQ ID:34212, to the nucleotide sequence of VGAM152 RNA, herein designated

VGAM RNA, also designated SEQ ID:2863.

[11002] Another function of VGAM152 is therefore inhibition of KIAA1102 (Accession XM_044461). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1102. KIAA1223 (Accession XM_048747) is another VGAM152 host target gene. KIAA1223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1223 BINDING SITE, designated SEQ ID:35245, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11003] Another function of VGAM152 is therefore inhibition of KIAA1223 (Accession XM_048747). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. KIAA1467 (Accession XM_049605) is another VGAM152 host target gene. KIAA1467 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1467, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1467 BINDING SITE, designated SEQ ID:35453, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11004] Another function of VGAM152 is therefore inhibition of KIAA1467 (Accession XM_049605). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1467. MGC12966 (Accession NM_032706) is another VGAM152 host target gene. MGC12966 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12966 BINDING SITE, designated SEQ ID:26419, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11005] Another function of VGAM152 is therefore inhibition of MGC12966 (Accession NM_032706). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC12966. MGC2306 (Accession NM_032638) is another VGAM152 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26353, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11006] Another function of VGAM152 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM_014182) is another VGAM152 host target gene. ORMDL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ORMDL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ORMDL2 BINDING SITE, designated SEQ

ID:15467, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11007] Another function of VGAM152 is therefore inhibition of ORM1-like 2 (*S. cerevisiae*) (ORMDL2, Accession NM_014182). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ORMDL2. P66 (Accession NM_020699) is another VGAM152 host target gene. P66 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by P66, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P66 BINDING SITE, designated SEQ ID:21844, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11008] Another function of VGAM152 is therefore inhibition of P66 (Accession NM_020699). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P66. PRO0159 (Accession NM_014118) is another VGAM152 host target gene. PRO0159 BINDING SITE is HOST TARGET

binding site found in the 5' untranslated region of mRNA encoded by PRO0159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0159 BINDING SITE, designated SEQ ID:15372, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11009] Another function of VGAM152 is therefore inhibition of PRO0159 (Accession NM_014118). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0159. LOC144740 (Accession XM_084959) is another VGAM152 host target gene. LOC144740 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144740, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144740 BINDING SITE, designated SEQ ID:37786, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11010] Another function of VGAM152 is therefore inhibition of

LOC144740 (Accession XM_084959). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144740. LOC145820 (Accession XM_085246) is another VGAM152 host target gene. LOC145820 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145820, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145820 BINDING SITE, designated SEQ ID:37994, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11011] Another function of VGAM152 is therefore inhibition of LOC145820 (Accession XM_085246). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145820. LOC148195 (Accession XM_097419) is another VGAM152 host target gene. LOC148195 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC148195 BINDING SITE, designated SEQ ID:40873, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11012] Another function of VGAM152 is therefore inhibition of LOC148195 (Accession XM_097419). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148195. LOC148811 (Accession XM_086326) is another VGAM152 host target gene. LOC148811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148811 BINDING SITE, designated SEQ ID:38598, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11013] Another function of VGAM152 is therefore inhibition of LOC148811 (Accession XM_086326). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148811. LOC148930 (Accession XM_086369) is an-

other VGAM152 host target gene. LOC148930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148930 BINDING SITE, designated SEQ ID:38619, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11014] Another function of VGAM152 is therefore inhibition of LOC148930 (Accession XM_086369). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148930. LOC149706 (Accession XM_097718) is another VGAM152 host target gene. LOC149706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149706 BINDING SITE, designated SEQ ID:41059, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11015] Another function of VGAM152 is therefore inhibition of LOC149706 (Accession XM_097718). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149706. LOC152765 (Accession XM_087519) is another VGAM152 host target gene. LOC152765 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152765, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152765 BINDING SITE, designated SEQ ID:39319, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11016] Another function of VGAM152 is therefore inhibition of LOC152765 (Accession XM_087519). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152765. LOC157247 (Accession XM_088275) is another VGAM152 host target gene. LOC157247 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157247, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157247 BINDING SITE, designated SEQ ID:39574, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11017] Another function of VGAM152 is therefore inhibition of LOC157247 (Accession XM_088275). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157247. LOC201164 (Accession XM_113904) is another VGAM152 host target gene. LOC201164 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201164 BINDING SITE, designated SEQ ID:42532, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11018] Another function of VGAM152 is therefore inhibition of LOC201164 (Accession XM_113904). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC201164. LOC221738 (Accession XM_168097) is another VGAM152 host target gene. LOC221738 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221738, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221738 BINDING SITE, designated SEQ ID:45029, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11019] Another function of VGAM152 is therefore inhibition of LOC221738 (Accession XM_168097). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221738. LOC221935 (Accession XM_166537) is another VGAM152 host target gene. LOC221935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221935 BINDING SITE, designated SEQ ID:44499, to the nucleotide sequence of VGAM152 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2863.

[11020] Another function of VGAM152 is therefore inhibition of LOC221935 (Accession XM_166537). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221935. LOC222128 (Accession XM_166560) is another VGAM152 host target gene. LOC222128 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222128 BINDING SITE, designated SEQ ID:44541, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11021] Another function of VGAM152 is therefore inhibition of LOC222128 (Accession XM_166560). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222128. LOC253639 (Accession XM_171060) is another VGAM152 host target gene. LOC253639 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253639, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253639 BINDING SITE, designated SEQ ID:45854, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11022] Another function of VGAM152 is therefore inhibition of LOC253639 (Accession XM_171060). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253639. LOC91807 (Accession XM_040819) is another VGAM152 host target gene. LOC91807 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91807, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91807 BINDING SITE, designated SEQ ID:33385, to the nucleotide sequence of VGAM152 RNA, herein designated VGAM RNA, also designated SEQ ID:2863.

[11023] Another function of VGAM152 is therefore inhibition of LOC91807 (Accession XM_040819). Accordingly, utilities of VGAM152 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC91807. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 153 (VGAM153) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11024] VGAM153 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM153 was detected is described hereinabove with reference to Figs. 1–8.

[11025] VGAM153 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11026] VGAM153 gene encodes a VGAM153 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM153 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM153 precursor RNA is designated SEQ

ID:139, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:139 is located at position 49690 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11027] VGAM153 precursor RNA folds onto itself, forming VGAM153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11028] An enzyme complex designated DICER COMPLEX, `dices` the VGAM153 folded precursor RNA into VGAM153 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM153 RNA is designated SEQ ID:2864, and

is provided hereinbelow with reference to the sequence listing part.

[11029] VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM153 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11030] VGAM153 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM153 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM153 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11031] The complementary binding of VGAM153 RNA, herein designated VGAM RNA, to host target binding sites on VGAM153 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM153 host target RNA into VGAM153 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11032] It is appreciated that VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM153 host target genes. The mRNA of each one of this plurality of VGAM153 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM153 RNA, herein designated VGAM RNA, and which when bound by VGAM153 RNA causes inhibition of translation of respective one or more VGAM153 host target proteins.

[11033] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM153 gene, herein designated VGAM GENE, on one or more VGAM153 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11034] It is yet further appreciated that a function of VGAM153 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM153 correlate with, and may be deduced from, the identity of the host target genes which VGAM153 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11035] Nucleotide sequences of the VGAM153 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM153 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM153 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM153 are further described hereinbelow with reference to Table 1.

[11036] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM153 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM153 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11037] As mentioned hereinabove with reference to Fig. 1, a function of VGAM153 gene, herein designated VGAM is inhibition of expression of VGAM153 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM153 correlate with, and may be deduced from, the identity of the target genes which VGAM153 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11038] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974) is a VGAM153 host target gene. AKAP13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:43178, to the nucleotide sequence of VGAM153 RNA, herein designated VGAM RNA, also designated SEQ ID:2864.

[11039] A function of VGAM153 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession XM_116974), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17.FLJ12700 (Accession NM_024910) is another VGAM153 host target gene. FLJ12700 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12700 BINDING SITE, designated SEQ ID:24412, to the nucleotide sequence of VGAM153 RNA, herein designated VGAM RNA, also designated SEQ ID:2864.

[11040] Another function of VGAM153 is therefore inhibition of FLJ12700 (Accession NM_024910). Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12700. Hippocalcin Like 4 (HPCAL4, Accession NM_016257) is another VGAM153 host target gene. HPCAL4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HPCAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCAL4 BINDING SITE, designated SEQ ID:18385, to the nucleotide sequence of VGAM153 RNA, herein designated VGAM RNA, also designated SEQ ID:2864.

[11041] Another function of VGAM153 is therefore inhibition of Hippocalcin Like 4 (HPCAL4, Accession NM_016257). Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL4. LOC146243 (Accession XM_096956) is another VGAM153 host target gene. LOC146243 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146243 BINDING SITE, designated SEQ ID:40673, to the nucleotide sequence of VGAM153 RNA, herein designated VGAM RNA, also designated SEQ ID:2864.

[11042] Another function of VGAM153 is therefore inhibition of LOC146243 (Accession XM_096956). Accordingly, utilities of VGAM153 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC146243. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 154 (VGAM154) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11043] VGAM154 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM154 was detected is described hereinabove with reference to Figs. 1–8.

[11044] VGAM154 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11045] VGAM154 gene encodes a VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM154 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM154 precursor RNA is designated SEQ

ID:140, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:140 is located at position 33147 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11046] VGAM154 precursor RNA folds onto itself, forming VGAM154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11047] An enzyme complex designated DICER COMPLEX, `dices` the VGAM154 folded precursor RNA into VGAM154 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM154 RNA is designated SEQ ID:2865, and

is provided hereinbelow with reference to the sequence listing part.

[11048] VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM154 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11049] VGAM154 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM154 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM154 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11050] The complementary binding of VGAM154 RNA, herein designated VGAM RNA, to host target binding sites on VGAM154 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM154 host target RNA into VGAM154 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11051] It is appreciated that VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM154 host target genes. The mRNA of each one of this plurality of VGAM154 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM154 RNA, herein designated VGAM RNA, and which when bound by VGAM154 RNA causes inhibition of translation of respective one or more VGAM154 host target proteins.

[11052] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM154 gene, herein designated VGAM GENE, on one or more VGAM154 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11053] It is yet further appreciated that a function of VGAM154 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM154 correlate with, and may be deduced from, the identity of the host target genes which VGAM154 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11054] Nucleotide sequences of the VGAM154 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM154 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM154 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM154 are further described hereinbelow with reference to Table 1.

[11055] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM154 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM154 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11056] As mentioned hereinabove with reference to Fig. 1, a function of VGAM154 gene, herein designated VGAM is inhibition of expression of VGAM154 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM154 correlate with, and may be deduced from, the identity of the target genes which VGAM154 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11057] MDM1 (Accession NM_020128) is a VGAM154 host target gene. MDM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MDM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MDM1 BINDING SITE, designated SEQ ID:21322, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11058] A function of VGAM154 is therefore inhibition of MDM1 (Accession NM_020128). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MDM1. Tumor Necrosis Factor Receptor Superfamily, Member 8

(TNFRSF8, Accession NM_001243) is another VGAM154 host target gene. TNFRSF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFRSF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFRSF8 BINDING SITE, designated SEQ ID:6911, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11059] Another function of VGAM154 is therefore inhibition of Tumor Necrosis Factor Receptor Superfamily, Member 8 (TNFRSF8, Accession NM_001243), a gene which regulates gene expression through activation of nf-kappab. Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFRSF8. The function of TNFRSF8 has been established by previous studies. By in vitro binding, immunoprecipitation, immunoblot, and yeast 2-hybrid analyses, Aizawa et al. (1997) showed that TRAF2 (OMIM Ref. No. 601895) and TRAF5 (OMIM Ref. No. 602356) interact with overlapping but distinct sequences in the C-terminal region of CD30 and mediate the activation of nuclear fac-

tor kappa-B (see OMIM Ref. No. 164011). Kurts et al. (1999) identified a new mechanism that protects against autoimmunity mediated through CD30. CD30 is expressed by activated, but not by resting, B or T cells. Using a model system in which ovalbumin-specific CD8+ T cells from the OT-I transgenic line were adoptively transferred into unirradiated transgenic mice that expressed ovalbumin in the pancreatic beta cells and the proximal renal tubular cells, Kurts et al. (1999) found that wildtype OT-I cells caused diabetes only when adoptively transferred in large numbers (greater than 250,000), with lower doses being effectively tolerized. CD30-deficient islet-specific CD8+ T cells were roughly 6,000-fold more autoaggressive than wildtype cells, with the transfer of as few as 160 CD30-deficient T cells leading to the complete destruction of pancreatic islets and the rapid onset of diabetes (within 4 days). Kurts et al. (1999) showed that in the absence of CD30 signaling, cells activated but not yet deleted by the CD95 (OMIM Ref. No. 134637)-dependent cross-tolerance mechanism gain the ability to proliferate extensively upon secondary encounter with antigen on parenchymal tissues, such as the pancreatic islets. Thus, CD30 signaling limits the proliferative potential of autore-

active CD8 effector T cells, and protects the body against autoimmunity.

[11060] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11061] Aizawa, S.; Nakano, H.; Ishida, T.; Horie, R.; Nagai, M.; Ito, K.; Yagita, H.; Okumura, K.; Inoue, J.; Watanabe, T. : Tumor necrosis factor receptor-associated factor (TRAF) 5 and TRAF2 are involved in CD30-mediated NF-kappa-B activation. J. Biol. Chem. 272: 2042-2045, 1997. ; and

[11062] Kurts, C.; Carbone, F. R.; Krummel, M. F.; Koch, K. M.; Miller, J. F. A. P.; Heath, W. R. : Signalling through CD30 protects against autoimmune diabetes mediated by CD8 T cells. Nature 3.

[11063] Further studies establishing the function and utilities of TNFRSF8 are found in John Hopkins OMIM database record ID 153243, and in cited publications numbered 11509-11510, 347 and 11511-11513 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ13114 (Accession NM_024541) is another VGAM154 host target gene. FLJ13114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13114, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13114 BINDING SITE, designated SEQ ID:23751, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11064] Another function of VGAM154 is therefore inhibition of FLJ13114 (Accession NM_024541). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13114. HCA4 (Accession XM_085287) is another VGAM154 host target gene. HCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCA4 BINDING SITE, designated SEQ ID:38025, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11065] Another function of VGAM154 is therefore inhibition of HCA4 (Accession XM_085287). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with HCA4. Insulin-like Growth Factor 2, Antisense (IGF2AS, Accession NM_016412) is another VGAM154 host target gene. IGF2AS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IGF2AS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2AS BINDING SITE, designated SEQ ID:18542, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11066] Another function of VGAM154 is therefore inhibition of Insulin-like Growth Factor 2, Antisense (IGF2AS, Accession NM_016412). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2AS. KIAA0476 (Accession NM_014856) is another VGAM154 host target gene. KIAA0476 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of KIAA0476 BINDING SITE, designated SEQ ID:16904, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11067] Another function of VGAM154 is therefore inhibition of KIAA0476 (Accession NM_014856). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0476. KIAA0652 (Accession NM_014741) is another VGAM154 host target gene. KIAA0652 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0652, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0652 BINDING SITE, designated SEQ ID:16410, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11068] Another function of VGAM154 is therefore inhibition of KIAA0652 (Accession NM_014741). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0652. KIAA0937 (Accession XM_166213) is another

VGAM154 host target gene. KIAA0937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0937 BINDING SITE, designated SEQ ID:44018, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11069] Another function of VGAM154 is therefore inhibition of KIAA0937 (Accession XM_166213). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0937. Signal Transducer and Activator of Transcription 2, 113kDa (STAT2, Accession NM_005419) is another VGAM154 host target gene. STAT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT2 BINDING SITE, designated SEQ ID:11892, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2865.

[11070] Another function of VGAM154 is therefore inhibition of Signal Transducer and Activator of Transcription 2, 113kDa (STAT2, Accession NM_005419). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT2. LOC145123 (Accession XM_041473) is another VGAM154 host target gene. LOC145123 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145123 BINDING SITE, designated SEQ ID:33533, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11071] Another function of VGAM154 is therefore inhibition of LOC145123 (Accession XM_041473). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145123. LOC151512 (Accession XM_098072) is another VGAM154 host target gene. LOC151512 BINDING SITE is HOST TARGET binding site found in the 5` un-

translated region of mRNA encoded by LOC151512, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151512 BINDING SITE, designated SEQ ID:41363, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11072] Another function of VGAM154 is therefore inhibition of LOC151512 (Accession XM_098072). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151512. LOC220549 (Accession XM_167521) is another VGAM154 host target gene. LOC220549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220549 BINDING SITE, designated SEQ ID:44649, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11073] Another function of VGAM154 is therefore inhibition of LOC220549 (Accession XM_167521). Accordingly, utilities

of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220549. LOC220827 (Accession XM_166052) is another VGAM154 host target gene. LOC220827 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220827, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220827 BINDING SITE, designated SEQ ID:43846, to the nucleotide sequence of VGAM154 RNA, herein designated VGAM RNA, also designated SEQ ID:2865.

[11074] Another function of VGAM154 is therefore inhibition of LOC220827 (Accession XM_166052). Accordingly, utilities of VGAM154 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220827. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 155 (VGAM155) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11075] VGAM155 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM155 was detected is described hereinabove with reference to Figs. 1–8.

[11076] VGAM155 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11077] VGAM155 gene encodes a VGAM155 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM155 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM155 precursor RNA is designated SEQ ID:141, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:141 is located at position 234589 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11078] VGAM155 precursor RNA folds onto itself, forming VGAM155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[11079] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM155 folded precursor RNA into VGAM155 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 45%) nucleotide se-
quence of VGAM155 RNA is designated SEQ ID:2866, and
is provided hereinbelow with reference to the sequence
listing part.

[11080] VGAM155 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM155 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM155 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[11081] VGAM155 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM155 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM155 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[11082] The complementary binding of VGAM155 RNA, herein designated VGAM RNA, to host target binding sites on VGAM155 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM155 host target RNA into VGAM155 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11083] It is appreciated that VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM155 host target genes. The mRNA of each one of this plurality of VGAM155 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM155 RNA, herein designated VGAM RNA, and which when bound by VGAM155 RNA causes inhibition of translation of respective one or more VGAM155 host target proteins.

[11084] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM155 gene, herein designated VGAM GENE, on one or

more VGAM155 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11085] It is yet further appreciated that a function of VGAM155 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM155 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM155 correlate with, and may be deduced from, the identity of the host target genes which VGAM155 binds and inhibits, and the function of these host target genes, as elaborated herein-

below.

- [11086] Nucleotide sequences of the VGAM155 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM155 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM155 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM155 are further described hereinbelow with reference to Table 1.
- [11087] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM155 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM155 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [11088] As mentioned hereinabove with reference to Fig. 1, a function of VGAM155 gene, herein designated VGAM is inhibition of expression of VGAM155 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM155 correlate with, and may be deduced from, the identity of the target genes which VGAM155 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

- [11089] Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349) is a VGAM155 host target gene. UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UBE2V1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2V1 BINDING SITE1 through UBE2V1 BINDING SITE3, designated SEQ ID:9374, SEQ ID:22526 and SEQ ID:22773 respectively, to the nucleotide sequence of VGAM155 RNA, herein designated VGAM RNA, also designated SEQ ID:2866.
- [11090] A function of VGAM155 is therefore inhibition of Ubiquitin-conjugating Enzyme E2 Variant 1 (UBE2V1, Accession NM_003349), a gene which may play a role in signaling for DNA repair. Accordingly, utilities of VGAM155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2V1. The function of UBE2V1 has been established by previous studies. Rothofsky and Lin (1997) isolated human brain cDNAs encoding UBE2V1, which they called CROC1. They identified 2 alternative 5-prime CROC1 cDNA sequences, which resulted in predicted 221- and 170-amino acid proteins that differ at

their N-terminal ends. The CROC1 isoforms have an acidic domain and a C-terminal basic domain. They show sequence similarity to ubiquitin-conjugating enzymes (UBCs, or E2s, e.g., UBE2D1; 602961) but lack the conserved cysteine residue that is critical for the catalytic activity of E2s. The CROC1 C-terminal domain has 42% sequence identity with the potential DNA-binding domain of TAFII250 (TAF2A; 313650). Immunofluorescence microscopy showed that recombinant CROC1 was located in the nucleus, excluding the nucleolar organizer regions. The authors demonstrated that CROC1 can cause transcriptional activation of the human FOS (OMIM Ref. No. 164810) promoter. Northern blot analysis detected approximately 2.1- and 2.5-kb CROC1 transcripts in all human tissues examined, with the highest levels in brain, skeletal muscle, and kidney. Sancho et al. (1998) isolated partial human intestinal epithelial cell cDNAs containing the 3-prime coding sequence and 3-prime untranslated region of UBE2V1, which they called UEV1. The UEV1 gene contains at least 6 exons and has at least 3 alternative polyadenylation sites in the 3-prime untranslated region. RT-PCR identified 4 alternatively spliced UEV1 transcripts that encode proteins with identical 90-amino acid C-

terminal sequences, including the region homologous to the conserved Ubc domain of E2 enzymes, but unique N-terminal sequences. The 140-amino acid C terminus of the deduced 221- and 170-amino acid UEV1 isoforms identified by Rothofsky and Lin (1997) is 90% identical to UEV2 (UBE2V2; 603001); it is 18%, 24%, and 22% identical to the Ubc domain of human UBE2I (OMIM Ref. No. 601661), *S. cerevisiae* UBC4 and UBC7, and *A. thaliana* UBC1, respectively. The authors showed that UEV1 does not have ubiquitin-conjugating activity in vitro. UEV1 transcripts were downregulated upon differentiation of a colon carcinoma cell line. Constitutive expression of exogenous UEV1 protein in these colon carcinoma cells inhibited their capacity to differentiate upon confluence and induced changes in their cell cycle behavior, which was associated with an inhibition of the mitotic kinase CDK1 (see OMIM Ref. No. CDC2; 116940).

[11091] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11092] Rothofsky, M. L.; Lin, S. L. : CROC-1 encodes a protein which mediates transcriptional activation of the human FOS promoter. *Gene* 195: 141-149, 1997. ; and

[11093] Sancho, E.; Vila, M. R.; Sanchez-Pulido, L.; Lozano, J. J.; Paciucci, R.; Nadal, M.; Fox, M.; Harvey, C.; Bercovich, B.; Loukili, N.; Ciechanover, A.; Lin, S. L.; Sanz, F.; Estivill, X.

[11094] Further studies establishing the function and utilities of UBE2V1 are found in John Hopkins OMIM database record ID 602995, and in cited publications numbered 9020–5411 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC157349 (Accession XM_088298) is another VGAM155 host target gene. LOC157349 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157349 BINDING SITE, designated SEQ ID:39586, to the nucleotide sequence of VGAM155 RNA, herein designated VGAM RNA, also designated SEQ ID:2866.

[11095] Another function of VGAM155 is therefore inhibition of LOC157349 (Accession XM_088298). Accordingly, utilities of VGAM155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157349. LOC170409 (Accession XM_096330) is an–

other VGAM155 host target gene. LOC170409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170409 BINDING SITE, designated SEQ ID:40315, to the nucleotide sequence of VGAM155 RNA, herein designated VGAM RNA, also designated SEQ ID:2866.

[11096] Another function of VGAM155 is therefore inhibition of LOC170409 (Accession XM_096330). Accordingly, utilities of VGAM155 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170409. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 156 (VGAM156) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11097] VGAM156 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM156 was detected is described

hereinabove with reference to Figs. 1–8.

[11098] VGAM156 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11099] VGAM156 gene encodes a VGAM156 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM156 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM156 precursor RNA is designated SEQ ID:142, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:142 is located at position 29183 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11100] VGAM156 precursor RNA folds onto itself, forming VGAM156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11101] An enzyme complex designated DICER COMPLEX, `dices` the VGAM156 folded precursor RNA into VGAM156 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM156 RNA is designated SEQ ID:2867, and is provided hereinbelow with reference to the sequence listing part.

[11102] VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM156 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11103] VGAM156 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM156 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM156 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[11104] The complementary binding of VGAM156 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM156 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM156 host target RNA into VGAM156 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11105] It is appreciated that VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM156 host target genes. The mRNA of each one of this plurality of VGAM156 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM156 RNA, herein designated VGAM RNA, and which when bound by VGAM156 RNA causes inhibition of translation of respective one or more VGAM156 host target proteins.

[11106] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM156 gene, herein designated VGAM GENE, on one or more VGAM156 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11107] It is yet further appreciated that a function of VGAM156 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM156 correlate with, and may be deduced from, the identity of the host target genes which VGAM156 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11108] Nucleotide sequences of the VGAM156 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM156 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM156 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM156 are further described hereinbelow with reference to Table 1.

[11109] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM156 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM156 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11110] As mentioned hereinabove with reference to Fig. 1, a function of VGAM156 gene, herein designated VGAM is inhibition of expression of VGAM156 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM156 correlate with, and may be deduced from, the identity of the target genes which VGAM156 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11111] ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028) is a VGAM156 host target gene. ATP11A BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by ATP11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP11A BINDING SITE, designated SEQ ID:37802, to the nucleotide sequence of VGAM156 RNA, herein designated VGAM RNA, also designated SEQ ID:2867.

[11112] A function of VGAM156 is therefore inhibition of ATPase, Class VI, Type 11A (ATP11A, Accession XM_085028). Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP11A. D12S2489E (Accession NM_007360) is another VGAM156 host target gene. D12S2489E BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by D12S2489E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D12S2489E BINDING SITE, designated SEQ ID:14292, to the nucleotide sequence of VGAM156 RNA, herein designated VGAM RNA, also designated SEQ ID:2867.

[11113] Another function of VGAM156 is therefore inhibition of

D12S2489E (Accession NM_007360), a gene which interacts in the inhibition and activation of NK cells. Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D12S2489E. The function of D12S2489E has been established by previous studies. Bauer et al. (1999) found that NKG2D is expressed on gamma/delta T cells, CD8-alpha (OMIM Ref. No. 186910)/-beta (OMIM Ref. No. 186730)-positive T cells, and natural killer cells and is a receptor for MICA (OMIM Ref. No. 600169). MICA binding to NKG2D activated cytolytic responses of gamma/delta T cells and NK cells against transfectants and epithelial tumor cells expressing MICA. The authors noted that these results define an activating immunoreceptor-MHC ligand interaction that may promote antitumor NK and T-cell responses. Wu et al. (1999) demonstrated that NKG2D and DAP10 (OMIM Ref. No. 604089) interact specifically to form an activating immunoreceptor complex. Sutherland et al. (2002) showed that an NKG2D fusion protein or antibody to NKG2D blocked the binding of UL16-binding proteins, or ULBPs (see OMIM Ref. No. ULBP1; 605697), and MICs to primary NK cells, indicating that NKG2D is the counterstructure for ULBPs. Immunoblot analysis showed

that ULBPs stimulate marked protein phosphorylation, notably of JAK2 (OMIM Ref. No. 147796) and STAT5 (see OMIM Ref. No. 604260), and induce activation of the ERK (see OMIM Ref. No. 601795) mitogen-activated protein kinase (MAPK) pathway. Immunoprecipitation analysis demonstrated that ULBP triggering induces phosphorylation of both the p85 (OMIM Ref. No. 171833) and p110 (OMIM Ref. No. 601232) subunits of phosphatidylinositol 3-kinase (PI3K) through DAP10, the NKG2D signaling partner. PI3K, in turn, was found to be required for ULBP-induced cytokine and chemokine production. In all cases, Sutherland et al. (2002) observed that ULBP3 (OMIM Ref. No. 605699) bound more weakly to NKG2D and induced weaker signaling responses than did ULBP2 (OMIM Ref. No. 605698) or ULBP1. Animal model experiments lend further support to the function of D12S2489E. Colucci et al. (2002) noted that humans with mutations in ZAP70 (OMIM Ref. No. 176947) have T-cell immunodeficiency, that mice lacking Zap70 have blocked T-cell development, and that mice lacking Syk (OMIM Ref. No. 600085) have a failure of B-cell development. NK cells express both molecules, which associate with immunoreceptor tyrosine-based activation motifs (ITAMs). Using mice deficient

in both Zap70 and Syk, Colucci et al. (2002) observed NK cell activity comparable to that in wildtype mice. The mutant cells expressed Nkg2d and were able to lyse targets with and without Nkg2d ligands in vitro and in vivo. However, wildtype cells, but not the double-deficient cells, responded to CD16 (OMIM Ref. No. 146740) and Ly49d (see OMIM Ref. No. 604274) cross-linking with increased cytotoxicity, suggesting that these 2 ITAM-bearing receptors are unable to signal in the mutant cells. Inhibitors of PI3K or Src kinases blocked and, in combination, abrogated cytotoxic activity in the mutant cells, whereas inhibition of both kinases was required to reduce wildtype NK activity. Colucci et al. (2002) concluded that intracellular signaling in the adaptive immune system, i.e., in B and T cells, is fundamentally different from that in the NK cells of the innate immune system.

[11114] It is appreciated that the abovementioned animal model for D12S2489E is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11115] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11116] Sutherland, C. L.; Chalupny, N. J.; Schooley, K.; Vanden-Bos, T.; Kubin, M.; Cosman, D. : UL16-binding proteins, novel MHC class I-related proteins, bind to NKG2D and activate multiple signaling pathways in primary NK cells. *J. Immun.* 168: 671-679, 2002. ; and
- [11117] Groh, V.; Rhinehart, R.; Randolph-Habecker, J.; Topp, M. S.; Riddell, S. R.; Spies, T. : Costimulation of CD8-alpha-beta T cells by NKG2D via engagement by MIC induced on virus-infected.
- [11118] Further studies establishing the function and utilities of D12S2489E are found in John Hopkins OMIM database record ID 602893, and in cited publications numbered 7909, 12705-7912, 7914, 7915, 8094-242 and 2528 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434N1511 (Accession XM_166138) is another VGAM156 host target gene. DKFZP434N1511 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434N1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N1511 BINDING SITE, designated SEQ ID:43933, to the nucleotide

sequence of VGAM156 RNA, herein designated VGAM RNA, also designated SEQ ID:2867.

[11119] Another function of VGAM156 is therefore inhibition of DKFZP434N1511 (Accession XM_166138). Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N1511. LOC56906 (Accession NM_020147) is another VGAM156 host target gene. LOC56906 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56906, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56906 BINDING SITE, designated SEQ ID:21342, to the nucleotide sequence of VGAM156 RNA, herein designated VGAM RNA, also designated SEQ ID:2867.

[11120] Another function of VGAM156 is therefore inhibition of LOC56906 (Accession NM_020147). Accordingly, utilities of VGAM156 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56906. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 157 (VGAM157) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11121] VGAM157 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM157 was detected is described hereinabove with reference to Figs. 1–8.

[11122] VGAM157 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11123] VGAM157 gene encodes a VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM157 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM157 precursor RNA is designated SEQ ID:143, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:143 is located at position 96551 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform

virus).

[11124] VGAM157 precursor RNA folds onto itself, forming VGAM157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11125] An enzyme complex designated DICER COMPLEX, `dices` the VGAM157 folded precursor RNA into VGAM157 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM157 RNA is designated SEQ ID:2868, and is provided hereinbelow with reference to the sequence listing part.

[11126] VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM157 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11127] VGAM157 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM157 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM157 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11128] The complementary binding of VGAM157 RNA, herein designated VGAM RNA, to host target binding sites on VGAM157 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM157 host target RNA into VGAM157 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11129] It is appreciated that VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM157 host target genes. The mRNA of each one of this plurality of VGAM157 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM157 RNA, herein designated VGAM RNA, and which when bound by VGAM157 RNA causes inhibition of translation of respective one or more VGAM157 host target proteins.

[11130] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM157 gene, herein designated VGAM GENE, on one or more VGAM157 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11131] It is yet further appreciated that a function of VGAM157 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific func-

tions, and accordingly utilities, of VGAM157 correlate with, and may be deduced from, the identity of the host target genes which VGAM157 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [11132] Nucleotide sequences of the VGAM157 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM157 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM157 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM157 are further described hereinbelow with reference to Table 1.
- [11133] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM157 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM157 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [11134] As mentioned hereinabove with reference to Fig. 1, a function of VGAM157 gene, herein designated VGAM is inhibition of expression of VGAM157 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM157 correlate with, and may be deduced from, the identity of the target genes which VGAM157 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11135] Adenylate Cyclase 2 (brain) (ADCY2, Accession XM_036383) is a VGAM157 host target gene. ADCY2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY2 BINDING SITE, designated SEQ ID:32433, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11136] A function of VGAM157 is therefore inhibition of Adenylate Cyclase 2 (brain) (ADCY2, Accession XM_036383), a gene which Adenylate cyclase (type 2), an ATP-pyrophosphate lyase; converts ATP to cAMP. Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY2. The function of ADCY2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove

with reference to VGAM120. Collagen, Type IV, Alpha 4 (COL4A4, Accession NM_000092) is another VGAM157 host target gene. COL4A4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A4 BINDING SITE, designated SEQ ID:5552, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11137] Another function of VGAM157 is therefore inhibition of Collagen, Type IV, Alpha 4 (COL4A4, Accession NM_000092). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A4. Fyn-related Kinase (FRK, Accession NM_002031) is another VGAM157 host target gene. FRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRK BINDING SITE, designated SEQ

ID:7787, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11138] Another function of VGAM157 is therefore inhibition of Fyn-related Kinase (FRK, Accession NM_002031), a gene which binds pRb (RB1) during G1 and S phase and suppresses growth. Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FRK. The function of FRK has been established by previous studies. Tyrosine kinases are either expressed cytoplasmically, such as SRC (CSK; 124095), or as transmembrane receptors, such as growth factor receptors. They are involved in signal transduction and the regulation of cellular proliferation and have been linked to tumorigenesis through overexpression or mutation. Anneren et al. (2000) showed that expression of Gtk, the rodent homolog of FRK, in a rat pheochromocytoma cell line used as a model for neuronal cell differentiation induced nerve growth factor (see OMIM Ref. No. 162030)-independent neurite outgrowth and Rap1 (OMIM Ref. No. 605061) activation, probably through activation of the CrkII (OMIM Ref. No. 164762)-C3G (GRF2; 600303) pathway.

- [11139] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [11140] Anneren, C.; Reedquist, K. A.; Bos, J. L.; Welsh, M. : GTK, a Src-related tyrosine kinase, induces nerve growth factor-independent neurite outgrowth in PC12 cells through activation of the Rap1 pathway: relationship to Shb tyrosine phosphorylation and elevated levels of focal adhesion kinase. *J. Biol. Chem.* 275: 29153–29161, 2000. ; and
- [11141] Cance, W. G.; Craven, R. J.; Bergman, M.; Xu, L.; Alitalo, K.; Liu, E. T. : Rak, a novel nuclear tyrosine kinase expressed in epithelial cells. *Cell Growth Differ.* 5: 1347–1355, 1994.
- [11142] Further studies establishing the function and utilities of FRK are found in John Hopkins OMIM database record ID 606573, and in cited publications numbered 6108–6112 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 2 (A1–5) (ZNF2, Accession NM_021088) is another VGAM157 host target gene. ZNF2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of ZNF2 BINDING SITE, designated SEQ ID:22067, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11143] Another function of VGAM157 is therefore inhibition of Zinc Finger Protein 2 (A1-5) (ZNF2, Accession NM_021088). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF2. DKFZP727G051 (Accession XM_045308) is another VGAM157 host target gene. DKFZP727G051 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP727G051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727G051 BINDING SITE, designated SEQ ID:34428, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11144] Another function of VGAM157 is therefore inhibition of DKFZP727G051 (Accession XM_045308). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP727G051. Enabled Homolog (Drosophila) (ENAH, Accession NM_018212) is another VGAM157 host target gene. ENAH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENAH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENAH BINDING SITE, designated SEQ ID:20127, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11145] Another function of VGAM157 is therefore inhibition of Enabled Homolog (Drosophila) (ENAH, Accession NM_018212). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENAH. KIAA1237 (Accession XM_087386) is another VGAM157 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ

ID:39218, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11146] Another function of VGAM157 is therefore inhibition of KIAA1237 (Accession XM_087386). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. Lymphoid-restricted Membrane Protein (LRMP, Accession NM_006152) is another VGAM157 host target gene. LRMP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRMP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRMP BINDING SITE, designated SEQ ID:12807, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11147] Another function of VGAM157 is therefore inhibition of Lymphoid-restricted Membrane Protein (LRMP, Accession NM_006152). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRMP. MOST2 (Accession NM_020250) is another VGAM157 host target gene.

MOST2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOST2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOST2 BINDING SITE, designated SEQ ID:21556, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11148] Another function of VGAM157 is therefore inhibition of MOST2 (Accession NM_020250). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOST2. Paralemmin (PALM, Accession NM_002579) is another VGAM157 host target gene. PALM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PALM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PALM BINDING SITE, designated SEQ ID:8441, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11149] Another function of VGAM157 is therefore inhibition of Paralemmin (PALM, Accession NM_002579). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PALM. LOC197285 (Accession XM_113752) is another VGAM157 host target gene. LOC197285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197285 BINDING SITE, designated SEQ ID:42415, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11150] Another function of VGAM157 is therefore inhibition of LOC197285 (Accession XM_113752). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197285. LOC92283 (Accession XM_044049) is another VGAM157 host target gene. LOC92283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92283, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92283 BINDING SITE, designated SEQ ID:34093, to the nucleotide sequence of VGAM157 RNA, herein designated VGAM RNA, also designated SEQ ID:2868.

[11151] Another function of VGAM157 is therefore inhibition of LOC92283 (Accession XM_044049). Accordingly, utilities of VGAM157 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92283. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 158 (VGAM158) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11152] VGAM158 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM158 was detected is described hereinabove with reference to Figs. 1–8.

[11153] VGAM158 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM158 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11154] VGAM158 gene encodes a VGAM158 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM158 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM158 precursor RNA is designated SEQ ID:144, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:144 is located at position 216380 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11155] VGAM158 precursor RNA folds onto itself, forming VGAM158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11156] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM158 folded precursor RNA into VGAM158 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM158 RNA is designated SEQ ID:2869, and is provided hereinbelow with reference to the sequence listing part.

[11157] VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM158 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11158] VGAM158 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM158 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM158 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11159] The complementary binding of VGAM158 RNA, herein designated VGAM RNA, to host target binding sites on VGAM158 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM158 host target RNA into VGAM158 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11160] It is appreciated that VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM158 host target genes. The mRNA of each one of this plurality of VGAM158 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM158 RNA, herein designated VGAM RNA, and which when bound by VGAM158 RNA causes inhibition of translation of respective one or more VGAM158 host target proteins.

[11161] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM158 gene, herein designated VGAM GENE, on one or more VGAM158 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11162] It is yet further appreciated that a function of VGAM158 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM158 correlate with, and may be deduced from, the identity of the host target genes which VGAM158 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11163] Nucleotide sequences of the VGAM158 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM158 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM158 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM158 are further

described hereinbelow with reference to Table 1.

[11164] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM158 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM158 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11165] As mentioned hereinabove with reference to Fig. 1, a function of VGAM158 gene, herein designated VGAM is inhibition of expression of VGAM158 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM158 correlate with, and may be deduced from, the identity of the target genes which VGAM158 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11166] HERV-H LTR-associating 1 (HHLA1, Accession NM_005712) is a VGAM158 host target gene. HHLA1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HHLA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of HHLA1 BINDING SITE, designated SEQ ID:12265, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11167] A function of VGAM158 is therefore inhibition of HERV-H LTR-associating 1 (HHLA1, Accession NM_005712), a gene which has unknown function and with low similarity to a region of *S. cerevisiae* WSC4. Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HHLA1. The function of HHLA1 has been established by previous studies. Human endogenous retroviruses (HERVs) are repetitive elements, derived from ancient germline retroviral infections, that have increased in copy number by further rounds of infection, retrotransposition, and/or duplication. The HERV-H family has been shown to play a role in the expression of a variety of adjacent genes. For example, Feuchter-Murthy et al. (1993) isolated a teratocarcinoma cell line transcript, PLA2L (phospholipase A2-like), which initiates in the long terminal repeat (LTR) of an HERV-H element present in an intron and splices into downstream exons. They found that the teratocarcinoma cells contained additional, alternatively spliced PLA2L mRNAs, designated AF6 through -8, which lack the

coding regions for the phospholipase A2 (PLA2)–like domains. Kowalski et al. (1999) determined that PLA2L is a tripartite fusion transcript expressed from the HERV–H element's promoter and containing exons from a novel gene, HHLA1, and from OC90 (OMIM Ref. No. 601658), a gene encoding an inner ear protein with PLA2 domains. The coding regions of the AF6, –7, and –8 mRNAs are derived only from the HHLA1 gene and encode a predicted 305–amino acid protein. The authors hypothesized that the human HHLA1 and OC90 genes are normally expressed independently from different promoters, and that the intergenic splicing event that generates PLA2L is specific to teratocarcinoma cells. The HERV–H element is located within an intron of HHLA1 and the OC90 gene is located less than 10 kb downstream of HHLA1. Kowalski et al. (1997) determined that the HERV–H element at this locus integrated 15 to 20 million years ago since it is present in chimpanzee and gorilla but absent in orangutan and lower primates. They mapped the HHLA1 locus to 8q24.

[11168] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11169] Kowalski, P. E.; Freeman, J. D.; Mager, D. L. : Intergenic splicing between a HERV-H endogenous retrovirus and two adjacent human genes. *Genomics* 57: 371–379, 1999.
; and

[11170] Kowalski, P. E.; Freeman, J. D.; Nelson, D. T.; Mager, D. L. : Genomic structure and evolution of a novel gene (PLA2L) with duplicated phospholipase A2-like domains. *Genomics* 39: 38–46.

[11171] Further studies establishing the function and utilities of HHLA1 are found in John Hopkins OMIM database record ID 604109, and in cited publications numbered 6211–621 and 7061 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ13657 (Accession NM_024828) is another VGAM158 host target gene. FLJ13657 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13657, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13657 BINDING SITE, designated SEQ ID:24221, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11172] Another function of VGAM158 is therefore inhibition of FLJ13657 (Accession NM_024828). Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13657. LOC158629 (Accession XM_098972) is another VGAM158 host target gene. LOC158629 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158629, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158629 BINDING SITE, designated SEQ ID:42019, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11173] Another function of VGAM158 is therefore inhibition of LOC158629 (Accession XM_098972). Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158629. LOC169436 (Accession XM_095696) is another VGAM158 host target gene. LOC169436 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC169436, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169436 BINDING SITE, designated SEQ ID:40276, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11174] Another function of VGAM158 is therefore inhibition of LOC169436 (Accession XM_095696). Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169436. LOC255098 (Accession XM_170912) is another VGAM158 host target gene. LOC255098 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255098 BINDING SITE, designated SEQ ID:45688, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11175] Another function of VGAM158 is therefore inhibition of LOC255098 (Accession XM_170912). Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255098. LOC96597 (Accession XM_039922) is another VGAM158 host target gene. LOC96597 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC96597, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC96597 BINDING SITE, designated SEQ ID:33229, to the nucleotide sequence of VGAM158 RNA, herein designated VGAM RNA, also designated SEQ ID:2869.

[11176] Another function of VGAM158 is therefore inhibition of LOC96597 (Accession XM_039922). Accordingly, utilities of VGAM158 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC96597. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 159 (VGAM159) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11177] VGAM159 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM159 was detected is described hereinabove with reference to Figs. 1–8.

[11178] VGAM159 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11179] VGAM159 gene encodes a VGAM159 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM159 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM159 precursor RNA is designated SEQ ID:145, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:145 is located at position 40934 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11180] VGAM159 precursor RNA folds onto itself, forming VGAM159 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11181] An enzyme complex designated DICER COMPLEX, `dices` the VGAM159 folded precursor RNA into VGAM159 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 69%) nucleotide sequence of VGAM159 RNA is designated SEQ ID:2870, and is provided hereinbelow with reference to the sequence listing part.

[11182] VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM159 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11183] VGAM159 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM159 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM159 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11184] The complementary binding of VGAM159 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM159 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM159 host target RNA into VGAM159 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11185] It is appreciated that VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM159 host target genes. The mRNA of each one of this plurality of VGAM159 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM159 RNA, herein designated VGAM RNA, and which when bound by VGAM159 RNA causes inhibition of translation of respective one or more VGAM159 host target proteins.

[11186] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM159 gene, herein designated VGAM GENE, on one or more VGAM159 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11187] It is yet further appreciated that a function of VGAM159 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM159 correlate with, and may be deduced from, the identity of the host target genes which VGAM159 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11188] Nucleotide sequences of the VGAM159 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM159 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM159 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM159 are further
described hereinbelow with reference to Table 1.

[11189] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM159 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM159 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[11190] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM159 gene, herein designated VGAM is
inhibition of expression of VGAM159 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM159 correlate with, and may be deduced
from, the identity of the target genes which VGAM159
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[11191] Cyclin T2 (CCNT2, Accession NM_058241) is a VGAM159
host target gene. CCNT2 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by CCNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNT2 BINDING SITE, designated SEQ ID:27768, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11192] A function of VGAM159 is therefore inhibition of Cyclin T2 (CCNT2, Accession NM_058241), a gene which is a regulatory subunit of the cyclin-dependent kinase pair (cdk9/cyclin t) complex. Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNT2. The function of CCNT2 has been established by previous studies. Positive transcription elongation factor b (OMIM Ref. No. P-TEFb) is thought to facilitate the transition from abortive to productive elongation by phosphorylating the C-terminal domain (CTD) of the largest subunit of RNA polymerase II (POLR2A; 180660). Drosophila P-TEFb is composed of CDK9 (OMIM Ref. No. 603251) and cyclin T. By searching an EST database for homologs of Drosophila cyclin T, Peng et al. (1998) identified cDNAs encoding hu-

man cyclins T1 (OMIM Ref. No. 602506) and T2. Alternative splicing of the primary T2 transcript results in 2 isoforms termed T2a and T2b. The predicted 663-amino acid T2a and 730-amino acid T2b isoforms have different C-termini. Within the conserved N-terminal cyclin box region, cyclin T2 shares 64% and 81% identity with *Drosophila* cyclin T and human cyclin T1, respectively. Immunoprecipitation studies demonstrated that CDK9 is complexed with the cyclins T1 and T2 in HeLa cell nuclear extracts. Approximately 80% of CDK9 is complexed with cyclin T1, 10% with cyclin T2a and 10% with T2b. Each complex is an active P-TEFb molecule that can phosphorylate the CTD of RNA polymerase II and cause the transition from abortive elongation into productive elongation. When expressed in mammalian cells, all 3 CDK9/cyclin T combinations strongly activated a CMV promoter. Northern blot analysis revealed that cyclin T2 was expressed as multiple mRNAs in all human tissues tested. Yang et al. (2001) identified 7SK snRNA (OMIM Ref. No. 606515) as a specific P-TEFb-associated factor. 7SK inhibits general and HIV-1 Tat-specific transcriptional activities of P-TEFb in vivo and in vitro by inhibiting the kinase activity of CDK9 and preventing recruitment of P-TEFb to the HIV-1

promoter. 7SK is efficiently dissociated from P-TEFb (the CDK9/cyclin T1 heterodimer) by treatment of cells with ultraviolet irradiation and actinomycin D. As these 2 agents have been shown to enhance significantly HIV-1 transcription and phosphorylation of Pol-II, Yang et al. (2001) concluded that their data provide a mechanistic explanation for this stimulatory effect. Yang et al. (2001) further suggested that the 7SK/P-TEFb interaction may serve as a principal control point for the induction of cellular and HIV-1 viral gene expression during stress-related responses. The study demonstrated the involvement of an snRNA in controlling the activity of CDK/cyclin kinase.

[11193] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11194] Peng, J.; Zhu, Y.; Milton, J. T.; Price, D. H. : Identification of multiple cyclin subunits of human P-TEFb. *Genes Dev.* 12: 755-762, 1998. ; and

[11195] Yang, Z.; Zhu, Q.; Luo, K.; Zhou, Q. : The 7SK small nuclear RNA inhibits the CDK9/cyclin T1 kinase to control transcription. *Nature* 414: 317-322, 2001.

[11196] Further studies establishing the function and utilities of

CCNT2 are found in John Hopkins OMIM database record ID 603862, and in cited publications numbered 9033–9035 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is another VGAM159 host target gene. DISC1 BINDING SITE1 and DISC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DISC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE1 and DISC1 BINDING SITE2, designated SEQ ID:20732 and SEQ ID:20733 respectively, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11197] Another function of VGAM159 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with

various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.GRP3 (Accession NM_015376) is another VGAM159 host target gene. GRP3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GRP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRP3 BINDING SITE, designated SEQ ID:17673, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11198] Another function of VGAM159 is therefore inhibition of GRP3 (Accession NM_015376). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRP3. KIAA0205 (Accession NM_014873) is another VGAM159 host target gene. KIAA0205 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0205 BINDING SITE,

designated SEQ ID:17001, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11199] Another function of VGAM159 is therefore inhibition of KIAA0205 (Accession NM_014873). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0205. KIAA1237 (Accession XM_087386) is another VGAM159 host target gene. KIAA1237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1237 BINDING SITE, designated SEQ ID:39215, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11200] Another function of VGAM159 is therefore inhibition of KIAA1237 (Accession XM_087386). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1237. KIAA1789 (Accession XM_040486) is another VGAM159 host target gene. KIAA1789 BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1789, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1789 BINDING SITE, designated SEQ ID:33306, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11201] Another function of VGAM159 is therefore inhibition of KIAA1789 (Accession XM_040486). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1789. PA26 (Accession NM_014454) is another VGAM159 host target gene. PA26 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PA26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PA26 BINDING SITE, designated SEQ ID:15806, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11202] Another function of VGAM159 is therefore inhibition of

PA26 (Accession NM_014454). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PA26. PHD Finger Protein 5A (PHF5A, Accession NM_032758) is another VGAM159 host target gene. PHF5A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHF5A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHF5A BINDING SITE, designated SEQ ID:26501, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11203] Another function of VGAM159 is therefore inhibition of PHD Finger Protein 5A (PHF5A, Accession NM_032758). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHF5A. LOC126603 (Accession XM_060090) is another VGAM159 host target gene. LOC126603 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126603 BINDING SITE, designated SEQ ID:37151, to the nucleotide sequence of VGAM159 RNA, herein designated VGAM RNA, also designated SEQ ID:2870.

[11204] Another function of VGAM159 is therefore inhibition of LOC126603 (Accession XM_060090). Accordingly, utilities of VGAM159 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126603. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 160 (VGAM160) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11205] VGAM160 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM160 was detected is described hereinabove with reference to Figs. 1–8.

[11206] VGAM160 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM160 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11207] VGAM160 gene encodes a VGAM160 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM160 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM160 precursor RNA is designated SEQ ID:146, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:146 is located at position 76536 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11208] VGAM160 precursor RNA folds onto itself, forming VGAM160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11209] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM160 folded precursor RNA into VGAM160 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM160 RNA is designated SEQ ID:2871, and is provided hereinbelow with reference to the sequence listing part.

[11210] VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM160 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11211] VGAM160 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM160 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM160 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11212] The complementary binding of VGAM160 RNA, herein designated VGAM RNA, to host target binding sites on VGAM160 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM160 host target RNA into VGAM160 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11213] It is appreciated that VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM160 host target genes. The mRNA of each one of this plurality of VGAM160 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM160 RNA, herein designated VGAM RNA, and which when bound by VGAM160 RNA causes inhibition of translation of respective one or more VGAM160 host target proteins.

[11214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM160 gene, herein designated VGAM GENE, on one or more VGAM160 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11215] It is yet further appreciated that a function of VGAM160 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM160 correlate with, and may be deduced from, the identity of the host target genes which VGAM160 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11216] Nucleotide sequences of the VGAM160 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM160 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM160 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM160 are further

described hereinbelow with reference to Table 1.

[11217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM160 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM160 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11218] As mentioned hereinabove with reference to Fig. 1, a function of VGAM160 gene, herein designated VGAM is inhibition of expression of VGAM160 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM160 correlate with, and may be deduced from, the identity of the target genes which VGAM160 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11219] Collagen, Type IV, Alpha 6 (COL4A6, Accession NM_033641) is a VGAM160 host target gene. COL4A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL4A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of COL4A6 BINDING SITE, designated SEQ ID:27356, to the nucleotide sequence of VGAM160 RNA, herein designated VGAM RNA, also designated SEQ ID:2871.

[11220] A function of VGAM160 is therefore inhibition of Collagen, Type IV, Alpha 6 (COL4A6, Accession NM_033641). Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A6. FLJ14566 (Accession NM_032806) is another VGAM160 host target gene. FLJ14566 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14566, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14566 BINDING SITE, designated SEQ ID:26563, to the nucleotide sequence of VGAM160 RNA, herein designated VGAM RNA, also designated SEQ ID:2871.

[11221] Another function of VGAM160 is therefore inhibition of FLJ14566 (Accession NM_032806). Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14566. LOC143153 (Accession XM_084440) is another VGAM160

host target gene. LOC143153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143153 BINDING SITE, designated SEQ ID:37578, to the nucleotide sequence of VGAM160 RNA, herein designated VGAM RNA, also designated SEQ ID:2871.

[11222] Another function of VGAM160 is therefore inhibition of LOC143153 (Accession XM_084440). Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143153. LOC143154 (Accession XM_084441) is another VGAM160 host target gene. LOC143154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143154 BINDING SITE, designated SEQ ID:37585, to the nucleotide sequence of VGAM160 RNA, herein designated VGAM RNA, also designated SEQ ID:2871.

[11223] Another function of VGAM160 is therefore inhibition of LOC143154 (Accession XM_084441). Accordingly, utilities of VGAM160 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143154. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 161 (VGAM161) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11224] VGAM161 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM161 was detected is described hereinabove with reference to Figs. 1–8.

[11225] VGAM161 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11226] VGAM161 gene encodes a VGAM161 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM161 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM161 precursor RNA is designated SEQ ID:147, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:147 is located at position 96172 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11227] VGAM161 precursor RNA folds onto itself, forming VGAM161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11228] An enzyme complex designated DICER COMPLEX, `dices` the VGAM161 folded precursor RNA into VGAM161 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM161 RNA is designated SEQ ID:2872, and is provided hereinbelow with reference to the sequence listing part.

[11229] VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM161 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11230] VGAM161 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM161 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM161 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM161 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11231] The complementary binding of VGAM161 RNA, herein designated VGAM RNA, to host target binding sites on VGAM161 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM161 host target RNA into VGAM161 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11232] It is appreciated that VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM161 host target genes. The mRNA of each one of this plurality of VGAM161 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM161 RNA, herein designated VGAM RNA, and which when bound by VGAM161 RNA causes inhibition of translation of respective one or more VGAM161 host target proteins.

[11233] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM161 gene, herein designated VGAM GENE, on one or more VGAM161 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11234] It is yet further appreciated that a function of VGAM161 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM161 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM161 correlate with, and may be deduced from, the identity of the host target genes which VGAM161 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11235] Nucleotide sequences of the VGAM161 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM161 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM161 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM161 are further described hereinbelow with reference to Table 1.

[11236] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM161 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM161 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11237] As mentioned hereinabove with reference to Fig. 1, a function of VGAM161 gene, herein designated VGAM is inhibition of expression of VGAM161 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM161 correlate with, and may be deduced from, the identity of the target genes which VGAM161 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11238] FLJ10579 (Accession NM_018145) is a VGAM161 host target gene. FLJ10579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10579, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10579 BINDING SITE, designated SEQ ID:19945, to the nucleotide sequence of VGAM161 RNA, herein designated VGAM RNA, also designated SEQ ID:2872.

[11239] A function of VGAM161 is therefore inhibition of FLJ10579 (Accession NM_018145). Accordingly, utilities of VGAM161 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10579. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 162 (VGAM162) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11240] VGAM162 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM162 was detected is described hereinabove with reference to Figs. 1–8.

[11241] VGAM162 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM162 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11242] VGAM162 gene encodes a VGAM162 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM162 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM162 precursor RNA is designated SEQ ID:148, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:148 is located at position 173989 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11243] VGAM162 precursor RNA folds onto itself, forming VGAM162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11244] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM162 folded precursor RNA into VGAM162 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM162 RNA is designated SEQ ID:2873, and is provided hereinbelow with reference to the sequence listing part.

[11245] VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM162 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11246] VGAM162 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM162 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM162 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[11247] The complementary binding of VGAM162 RNA, herein designated VGAM RNA, to host target binding sites on VGAM162 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM162 host target RNA into VGAM162 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11248] It is appreciated that VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM162 host target genes. The mRNA of each one of this plurality of VGAM162 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM162 RNA, herein designated VGAM RNA, and which when bound by VGAM162 RNA causes inhibition of translation of respective one or more VGAM162 host target proteins.

[11249] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM162 gene, herein designated VGAM GENE, on one or more VGAM162 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11250] It is yet further appreciated that a function of VGAM162 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM162 correlate with, and may be deduced from, the identity of the host target genes which VGAM162 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11251] Nucleotide sequences of the VGAM162 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM162 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM162 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM162 are further

described hereinbelow with reference to Table 1.

[11252] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM162 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM162 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11253] As mentioned hereinabove with reference to Fig. 1, a function of VGAM162 gene, herein designated VGAM is inhibition of expression of VGAM162 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM162 correlate with, and may be deduced from, the identity of the target genes which VGAM162 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11254] Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM_003679) is a VGAM162 host target gene. KMO BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KMO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KMO BINDING SITE, designated SEQ ID:9779, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11255] A function of VGAM162 is therefore inhibition of Kynurenine 3-monooxygenase (kynurenine 3-hydroxylase) (KMO, Accession NM_003679), a gene which may play a role in encephalic photoreception. Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KMO. The function of KMO has been established by previous studies. Kynurenine 3-monooxygenase (KMO; EC 1.14.13.9) is an NADPH-dependent flavin monooxygenase that catalyzes the hydroxylation of the L-tryptophan metabolite L-kynurenine to form L-3-hydroxykynurenine. By screening a human liver cDNA library with a partial *Drosophila* KMO cDNA, Alberati-Giani et al. (1997) isolated cDNAs encoding human KMO. The predicted 486-amino acid human protein shares 47% sequence identity with *Drosophila* KMO. When expressed in mammalian cells, recombinant human KMO exhibited kinetic properties similar to those of the native human protein. Northern blot analysis revealed that human KMO is expressed as an approximately

2-kb mRNA in liver and placenta, and at lower levels in kidney. By comparing genomic and cDNA sequences, Halford et al. (2001) determined that the KMO gene contains at least 15 exons spanning approximately 68 kb. By genomic sequence analysis, Halford et al. (2001) determined that the KMO gene overlaps with the OPN3 gene (OMIM Ref. No. 606695) on chromosome 1q43 and that the 2 genes are transcribed from opposite strands.

[11256] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11257] Alberati-Giani, D.; Cesura, A. M.; Broger, C.; Warren, W. D.; Rover, S.; Malherbe, P. : Cloning and functional expression of human kynurenine 3-monooxygenase. FEBS Lett. 410: 407-412, 1997. ; and

[11258] Halford, S.; Freedman, M. S.; Bellingham, J.; Inglis, S. L.; Poopalasundaram, S.; Soni, B. G.; Foster, R. G.; Hunt, D. M. : Characterization of a novel human opsin gene with wide tissue.

[11259] Further studies establishing the function and utilities of KMO are found in John Hopkins OMIM database record ID 603538, and in cited publications numbered 507 and 12220 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283) is another VGAM162 host target gene. TACC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TACC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TACC1 BINDING SITE, designated SEQ ID:12962, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11260] Another function of VGAM162 is therefore inhibition of Transforming, Acidic Coiled-coil Containing Protein 1 (TACC1, Accession NM_006283). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TACC1. FENS-1 (Accession NM_020830) is another VGAM162 host target gene. FENS-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FENS-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of FENS-1 BINDING SITE, designated SEQ ID:21890, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11261] Another function of VGAM162 is therefore inhibition of FENS-1 (Accession NM_020830). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FENS-1. FLJ10506 (Accession NM_018117) is another VGAM162 host target gene. FLJ10506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10506 BINDING SITE, designated SEQ ID:19888, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11262] Another function of VGAM162 is therefore inhibition of FLJ10506 (Accession NM_018117). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10506. KIAA1954 (Accession XM_085375) is another VGAM162

host target gene. KIAA1954 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1954, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1954 BINDING SITE, designated SEQ ID:38091, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11263] Another function of VGAM162 is therefore inhibition of KIAA1954 (Accession XM_085375). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1954. MGC32104 (Accession NM_144684) is another VGAM162 host target gene. MGC32104 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC32104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC32104 BINDING SITE, designated SEQ ID:29502, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11264] Another function of VGAM162 is therefore inhibition of MGC32104 (Accession NM_144684). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC32104. R3H Domain (binds single-stranded nucleic acids) Containing (R3HDM, Accession NM_015361) is another VGAM162 host target gene. R3HDM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by R3HDM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of R3HDM BINDING SITE, designated SEQ ID:17660, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11265] Another function of VGAM162 is therefore inhibition of R3H Domain (binds single-stranded nucleic acids) Containing (R3HDM, Accession NM_015361). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with R3HDM. LOC122509 (Accession NM_145249) is another VGAM162 host target gene. LOC122509 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC122509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122509 BINDING SITE, designated SEQ ID:29760, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11266] Another function of VGAM162 is therefore inhibition of LOC122509 (Accession NM_145249). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122509. LOC146138 (Accession XM_096938) is another VGAM162 host target gene. LOC146138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146138 BINDING SITE, designated SEQ ID:40658, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11267] Another function of VGAM162 is therefore inhibition of LOC146138 (Accession XM_096938). Accordingly, utilities

of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146138. LOC199958 (Accession XM_117163) is another VGAM162 host target gene. LOC199958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199958 BINDING SITE, designated SEQ ID:43265, to the nucleotide sequence of VGAM162 RNA, herein designated VGAM RNA, also designated SEQ ID:2873.

[11268] Another function of VGAM162 is therefore inhibition of LOC199958 (Accession XM_117163). Accordingly, utilities of VGAM162 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199958. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 163 (VGAM163) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11269] VGAM163 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM163 was detected is described hereinabove with reference to Figs. 1–8.

[11270] VGAM163 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11271] VGAM163 gene encodes a VGAM163 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM163 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM163 precursor RNA is designated SEQ ID:149, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:149 is located at position 110896 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11272] VGAM163 precursor RNA folds onto itself, forming VGAM163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[11273] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM163 folded precursor RNA into VGAM163 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM163 RNA is designated SEQ ID:2874, and
is provided hereinbelow with reference to the sequence
listing part.

[11274] VGAM163 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM163 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM163 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[11275] VGAM163 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM163 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM163 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[11276] The complementary binding of VGAM163 RNA, herein designated VGAM RNA, to host target binding sites on VGAM163 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM163 host target RNA into VGAM163 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11277] It is appreciated that VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM163 host target genes. The mRNA of each one of this plurality of VGAM163 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM163 RNA, herein designated VGAM RNA, and which when bound by VGAM163 RNA causes inhibition of translation of respective one or more VGAM163 host target proteins.

[11278] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM163 gene, herein designated VGAM GENE, on one or

more VGAM163 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11279] It is yet further appreciated that a function of VGAM163 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM163 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM163 correlate with, and may be deduced from, the identity of the host target genes which VGAM163 binds and inhibits, and the function of these host target genes, as elaborated herein-

below.

- [11280] Nucleotide sequences of the VGAM163 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM163 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM163 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM163 are further described hereinbelow with reference to Table 1.
- [11281] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM163 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM163 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [11282] As mentioned hereinabove with reference to Fig. 1, a function of VGAM163 gene, herein designated VGAM is inhibition of expression of VGAM163 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM163 correlate with, and may be deduced from, the identity of the target genes which VGAM163 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11283] ADP-ribosylation Factor 1 (ARF1, Accession XM_047545) is a VGAM163 host target gene. ARF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF1 BINDING SITE, designated SEQ ID:34992, to the nucleotide sequence of VGAM163 RNA, herein designated VGAM RNA, also designated SEQ ID:2874.

[11284] A function of VGAM163 is therefore inhibition of ADP-ribosylation Factor 1 (ARF1, Accession XM_047545). Accordingly, utilities of VGAM163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF1. LOC155438 (Accession XM_098722) is another VGAM163 host target gene. LOC155438 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155438 BINDING SITE, designated SEQ ID:41767, to the nucleotide sequence of VGAM163 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2874.

[11285] Another function of VGAM163 is therefore inhibition of LOC155438 (Accession XM_098722). Accordingly, utilities of VGAM163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155438. LOC56891 (Accession NM_020129) is another VGAM163 host target gene. LOC56891 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC56891, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56891 BINDING SITE, designated SEQ ID:21323, to the nucleotide sequence of VGAM163 RNA, herein designated VGAM RNA, also designated SEQ ID:2874.

[11286] Another function of VGAM163 is therefore inhibition of LOC56891 (Accession NM_020129). Accordingly, utilities of VGAM163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56891. LOC89919 (Accession XM_027244) is another VGAM163 host target gene. LOC89919 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC89919, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89919 BINDING SITE, designated SEQ ID:30467, to the nucleotide sequence of VGAM163 RNA, herein designated VGAM RNA, also designated SEQ ID:2874.

[11287] Another function of VGAM163 is therefore inhibition of LOC89919 (Accession XM_027244). Accordingly, utilities of VGAM163 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89919. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 164 (VGAM164) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11288] VGAM164 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM164 was detected is described hereinabove with reference to Figs. 1–8.

[11289] VGAM164 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syn–

drome Virus (white spot bacilliform virus). VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11290] VGAM164 gene encodes a VGAM164 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM164 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM164 precursor RNA is designated SEQ ID:150, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:150 is located at position 35494 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11291] VGAM164 precursor RNA folds onto itself, forming VGAM164 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11292] An enzyme complex designated DICER COMPLEX, `dices` the VGAM164 folded precursor RNA into VGAM164 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM164 RNA is designated SEQ ID:2875, and is provided hereinbelow with reference to the sequence listing part.

[11293] VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM164 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11294] VGAM164 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM164 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM164 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11295] The complementary binding of VGAM164 RNA, herein designated VGAM RNA, to host target binding sites on VGAM164 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM164 host tar-

get RNA into VGAM164 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11296] It is appreciated that VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM164 host target genes. The mRNA of each one of this plurality of VGAM164 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM164 RNA, herein designated VGAM RNA, and which when bound by VGAM164 RNA causes inhibition of translation of respective one or more VGAM164 host target proteins.

[11297] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM164 gene, herein designated VGAM GENE, on one or more VGAM164 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11298] It is yet further appreciated that a function of VGAM164 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM164 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM164 correlate with, and may be deduced from, the identity of the host target genes which VGAM164 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11299] Nucleotide sequences of the VGAM164 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM164 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM164 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM164 are further described hereinbelow with reference to Table 1.

[11300] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM164 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM164 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11301] As mentioned hereinabove with reference to Fig. 1, a function of VGAM164 gene, herein designated VGAM is inhibition of expression of VGAM164 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM164 correlate with, and may be deduced from, the identity of the target genes which VGAM164 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11302] Cyclin D2 (CCND2, Accession NM_001759) is a VGAM164 host target gene. CCND2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of CCND2 BINDING SITE, designated SEQ ID:7521, to the nucleotide sequence of VGAM164 RNA, herein designated VGAM RNA, also designated SEQ ID:2875.

[11303] A function of VGAM164 is therefore inhibition of Cyclin D2 (CCND2, Accession NM_001759), a gene which is essential for the control of the cell cycle at the g1/s (start) transition. Accordingly, utilities of VGAM164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND2. The function of CCND2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM128.EphA3 (EPHA3, Accession NM_005233) is another VGAM164 host target gene. EPHA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPHA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPHA3 BINDING SITE, designated SEQ ID:11740, to the nucleotide sequence of VGAM164 RNA, herein designated VGAM RNA, also designated SEQ ID:2875.

[11304] Another function of VGAM164 is therefore inhibition of EphA3 (EPHA3, Accession NM_005233), a gene which binds to ephrin-a2, -a3, -a4 and -a5. could play a role in lymphoid function. Accordingly, utilities of VGAM164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPHA3. The function of EPHA3 has been established by previous studies. See EPH (EPHA1; 179610) for background on Eph receptors and their ligands, the ephrins. Kinases that phosphorylate proteins on tyrosine residues (protein tyrosine kinases; PTKs) form a structurally related group of molecules that exhibit functional diversity. Genetic alterations that lead to the inappropriate activation or expression of PTKs may be oncogenic. Many growth factor receptors are PTKs, e.g., the receptors for epidermal growth factor (EGFR; 131550), platelet-derived growth factor (PDGFR1, 173410; PDGFR2, 173490), colony-stimulating factor-1 (CSF1R; 164770), and stem cell growth factor (OMIM Ref. No. 164920). Wicks et al. (1992) isolated and sequenced a 4.5-kb cDNA encoding the HEK receptor tyrosine kinase. Sequence comparison with other PTKs showed a high degree of homology with members of the EPH and ELK (EPHB1; 600600) families of receptor tyrosine kinases.

There was an apparent restriction of HEK expression to lymphoid tumor cell lines, raising the possibility that HEK may play a role in some human lymphoid malignancies and also in normal lymphoid function and differentiation. By purifying the protein from a pre-B acute lymphoblastic leukemia cell line and amino acid sequencing, Boyd et al. (1992) identified this molecule as a member of the eph/elk family of tyrosine kinases. They assigned this molecule the provisional name HEK, for human eph/elk-like kinase. By Southern blot analysis of somatic cell hybrids and fluorescence in situ hybridization, Wicks et al. (1994) localized the ETK gene to 3p11.2. Northern blotting by Fox et al. (1995) revealed that HEK4 is expressed as a single 7-kb transcript in a variety of human tissues, with the highest level of expression in placenta.

[11305] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11306] Wicks, I. P.; Wilkinson, D.; Salvaris, E.; Boyd, A. W. : Molecular cloning of HEK, the gene encoding a receptor tyrosine kinase expressed by human lymphoid tumor cell lines. Proc. Nat. Acad. Sci. 89: 1611-1615, 1992. ; and

[11307] Fox, G. M.; Holst, P. L.; Chute, H. T.; Lindberg, R. A.;

Janssen, A. M.; Basu, R.; Welcher, A. A. : cDNA cloning and tissue distribution of five human EPH-like receptor protein-tyrosine.

[11308] Further studies establishing the function and utilities of EPHA3 are found in John Hopkins OMIM database record ID 179611, and in cited publications numbered 12674-12677 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087) is another VGAM164 host target gene. UBE2G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G2 BINDING SITE, designated SEQ ID:32377, to the nucleotide sequence of VGAM164 RNA, herein designated VGAM RNA, also designated SEQ ID:2875.

[11309] Another function of VGAM164 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087), a gene which catalyzes the covalent attachment of ubiquitin to other pro-

teins. Accordingly, utilities of VGAM164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G2. The function of UBE2G2 has been established by previous studies. In eukaryotes, conjugation of target proteins to ubiquitin is an essential step in the proteasome-dependent degradation process and is mediated by a family of ubiquitin-conjugating (UBC) enzymes. See 600012. Katsanis and Fisher (1998) stated that *S. cerevisiae* Ubc7 is an endoplasmic reticulum-bound molecule whose active site faces the cytosol. Ubc7 has been shown to confer resistance to cadmium and to participate in the degradation of specific yeast proteins. As part of an effort to generate a transcriptional map of human chromosome 21, Katsanis and Fisher (1998) identified UBE2G2 cDNAs. The predicted 165-amino acid protein shares 60% sequence identity with yeast Ubc7. The nucleotide sequence of UBE2G2 is 57% similar to that of UBE2G (OMIM Ref. No. 601569), another human Ubc7 homolog. Northern blot analysis revealed that UBE2G2 is expressed ubiquitously as 2.9- and 7-kb mRNAs. The highest level of expression was seen in skeletal muscle. By inclusion within mapped clones and by analysis of somatic cell hybrid panels, Katsanis and Fisher (1998) mapped the

UBE2G2 gene to 21q22.3. Rose et al. (1998) confirmed the localization to 21q22.3 by FISH.

[11310] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11311] Katsanis, N.; Fisher, E. M. C. : Identification, expression, and chromosomal localization of ubiquitin conjugating enzyme 7 (UBE2G2), a human homologue of the *Saccharomyces cerevisiae* Ubc7 gene. *Genomics* 51: 128–131, 1998. ; and

[11312] Rose, S. A.; Leek, J. P.; Moynihan, T. P.; Ardley, H. C.; Markham, A. F.; Robinson, P. A. : Assignment of the ubiquitin conjugating enzyme gene, UBE2G2, to human chromosome band 21q22.3.

[11313] Further studies establishing the function and utilities of UBE2G2 are found in John Hopkins OMIM database record ID 603124, and in cited publications numbered 639–640 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP547E1010 (Accession NM_015607) is another VGAM164 host target gene. DKFZP547E1010 BINDING SITE1 and DKFZP547E1010 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

DKFZP547E1010, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP547E1010 BINDING SITE1 and DKFZP547E1010 BINDING SITE2, designated SEQ ID:17879 and SEQ ID:33243 respectively, to the nucleotide sequence of VGAM164 RNA, herein designated VGAM RNA, also designated SEQ ID:2875.

[11314] Another function of VGAM164 is therefore inhibition of DKFZP547E1010 (Accession NM_015607). Accordingly, utilities of VGAM164 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP547E1010. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 165 (VGAM165) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11315] VGAM165 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM165 was detected is described hereinabove with reference to Figs. 1–8.

[11316] VGAM165 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11317] VGAM165 gene encodes a VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM165 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM165 precursor RNA is designated SEQ ID:151, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:151 is located at position 293621 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11318] VGAM165 precursor RNA folds onto itself, forming VGAM165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11319] An enzyme complex designated DICER COMPLEX, `dices` the VGAM165 folded precursor RNA into VGAM165 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM165 RNA is designated SEQ ID:2876, and is provided hereinbelow with reference to the sequence listing part.

[11320] VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM165 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11321] VGAM165 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM165 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM165 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM165 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11322] The complementary binding of VGAM165 RNA, herein designated VGAM RNA, to host target binding sites on VGAM165 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM165 host target RNA into VGAM165 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11323] It is appreciated that VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM165 host target genes. The mRNA of each one of this plurality of VGAM165 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM165 RNA, herein designated VGAM RNA, and which when bound by VGAM165 RNA causes inhibition of translation of respective one or more VGAM165 host target proteins.

[11324] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM165 gene, herein designated VGAM GENE, on one or more VGAM165 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11325] It is yet further appreciated that a function of VGAM165 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM165 correlate with, and may be deduced from, the identity of the host target genes which VGAM165 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11326] Nucleotide sequences of the VGAM165 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM165 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM165 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM165 are further described hereinbelow with reference to Table 1.

[11327] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM165 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM165 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11328] As mentioned hereinabove with reference to Fig. 1, a function of VGAM165 gene, herein designated VGAM is inhibition of expression of VGAM165 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM165 correlate with, and may be deduced from, the identity of the target genes which VGAM165 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11329] Cell Division Cycle 25B (CDC25B, Accession NM_021873) is a VGAM165 host target gene. CDC25B BINDING SITE1 and CDC25B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

CDC25B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC25B BINDING SITE1 and CDC25B BINDING SITE2, designated SEQ ID:22411 and SEQ ID:22415 respectively, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11330] A function of VGAM165 is therefore inhibition of Cell Division Cycle 25B (CDC25B, Accession NM_021873), a gene which is positively activated by dephosphorylation. Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC25B. The function of CDC25B has been established by previous studies. Central to the onset of mitosis in all eukaryotic cells is the CDC2 protein kinase (CDK1; 116940), the activity of which is negatively regulated by phosphorylation and positively activated by dephosphorylation. The latter function is carried out by a specific phosphatase, CDC25. At least 3 human CDC25 genes code for the A, B, and C forms of CDC25. CDC25C (OMIM Ref. No. 157680) maps to chromosome 5. Lane et al. (1993) demonstrated by fluorescence in situ hybridiza-

tion that CDC25B maps to 20p13. PCR analysis of a monochromosomal hybrid cell panel yielded results supporting this chromosome assignment. Demetrick and Beach (1993) also mapped CDC25B to 20p13 by fluorescence in situ hybridization with confirmation by the polymerase chain reaction of hamster/human somatic cell hybrid DNA. Animal model experiments lend further support to the function of CDC25B. Lincoln et al. (2002) generated Cdc25b-deficient mice by targeted disruption and found that they were viable. As compared with wildtype cells, fibroblasts from Cdc25b $-/-$ mice grew vigorously in culture and arrested normally in response to DNA damage. Female Cdc25b $-/-$ mice were sterile and Cdc25b $-/-$ oocytes remained arrested at prophase with low maturation-promoting factor activity. Microinjection of wildtype Cdc25b mRNA into Cdc25b $-/-$ oocytes caused activation of maturation-promoting factor and resumption of meiosis. Thus, Lincoln et al. (2002) concluded that Cdc25b $-/-$ female mice were sterile because of permanent meiotic arrest resulting from the inability to activate the maturation-promoting factor component CDK1. Cdc25b is therefore essential for meiotic resumption in female mice. Lincoln et al. (2002) stated that mice lacking Cdc25b pro-

vided the first genetic model for studying the mechanisms regulating prophase arrest in vertebrates.

[11331] It is appreciated that the abovementioned animal model for CDC25B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11332] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11333] Lane, S. A.; Baker, E.; Sutherland, G. R.; Tonks, I.; Hayward, N.; Ellem, K. : The human cell cycle gene CDC25B is located at 20p13. Genomics 15: 693–694, 1993. ; and

[11334] Lincoln, A. J.; Wickramasinghe, D.; Stein, P.; Schultz, R. M.; Palko, M. E.; De Miguel, M. P.; Tessarollo, L.; Donovan, P. J. : Cdc25b phosphatase is required for resumption of meiosis d.

[11335] Further studies establishing the function and utilities of CDC25B are found in John Hopkins OMIM database record ID 116949, and in cited publications numbered 296 and 1936–1937 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glucose–6–phosphatase, Catalytic (glycogen storage disease type I, von Gierke disease) (G6PC, Accession

NM_000151) is another VGAM165 host target gene. G6PC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by G6PC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G6PC BINDING SITE, designated SEQ ID:5655, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11336] Another function of VGAM165 is therefore inhibition of Glucose-6-phosphatase, Catalytic (glycogen storage disease type I, von Gierke disease) (G6PC, Accession NM_000151). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G6PC. Mannosyl (alpha-1,3)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM_002406) is another VGAM165 host target gene. MGAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of MGAT1 BINDING SITE, designated SEQ ID:8225, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11337] Another function of VGAM165 is therefore inhibition of Mannosyl (alpha-1,3-)-glycoprotein Beta-1,2-N-acetylglucosaminyltransferase (MGAT1, Accession NM_002406), a gene which exists as a single protein-encoding exon. Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGAT1. The function of MGAT1 has been established by previous studies. There are believed to be over 100 different glycosyltransferases involved in the synthesis of protein-bound and lipid-bound oligosaccharides. One of these, UDP-N-acetylglucosamine:alpha-3-D-mannoside beta-1,2-N-acetylglucosaminyltransferase I (GlcNAc-T I; EC 2.4.1.101), is a medial-Golgi enzyme essential for the synthesis of hybrid and complex N-glycans. Kumar and Stanley (1989) identified the human gene encoding N-acetylglucosaminyltransferase I by complementation of the glycosylation defect in the Lec1 Chinese hamster ovary (CHO) cell mutant. Kumar et al. (1990) cloned the gene.

The overall features of the cDNA and deduced protein sequence (445 amino acids) were typical of other Golgi transferases that are type II transmembrane proteins. Hull et al. (1991) isolated 2 overlapping genomic DNA clones which span 18 kb containing the single 2.5-kb exon for GlcNAc-T I. The exon includes most of the 5-prime untranslated region, the complete coding sequence (1,335 bases, 445 amino acids), and the complete 3-prime untranslated region. Southern blot analysis indicated that the gene (symbolized GLCT1) exists in single copy in the human genome, and study of human-hamster somatic cell hybrids indicated that the gene is located on chromosome 5. Pownall et al. (1992) demonstrated that the sequence of the mouse gene *Mgat1* is highly conserved with respect to the human and rabbit homologs and exists as a single protein-encoding exon. They mapped the gene to mouse chromosome 11, closely linked to the gene encoding IL3 (OMIM Ref. No. 147740), by the analysis of multilocus interspecies backcrosses. Thus, the human gene may be in the same area as IL3, i.e., 5q23-q31. Kumar et al. (1992) mapped the gene to 5q31.2-q31.3 by in situ hybridization. Tan et al. (1995) reported that the MGAT1 gene maps to 5q35 by fluorescence in situ hybridization. They

considered the discrepancy with the findings of Kumar et al. (1992) to be due to greater precision of fluorescence analysis compared with radioactive in situ hybridization. Shows (1999) stated that by use of more sensitive FISH technology than that used in their 1992 report (Kumar et al., 1992), he and his colleagues confirmed the assignment of the MGAT1 gene to 5q35. On Northern blots, Yip et al. (1997) found that GlcNAc-T I is expressed as 2 mRNAs of 3.1 and 2.7 to 3.0 kb in all tissues tested, although only the 3.1-kb mRNA is seen in brain, and expression levels are low. Yip et al. (1997) also found that exon 1 of the GlcNAc-T I gene encodes the 5-prime untranslated region and contains multiple transcription start sites. Ioffe and Stanley (1994) produced transgenic mice lacking *Mgat1*. Homozygous mutant mice died between 9.5 and 10.5 days of development and were developmentally retarded, especially in neural tissue. Metzler et al. (1994) obtained similar results, finding that neural tube formation, vascularization, and left-right asymmetry formation were impaired in homozygous mutant mouse embryos.

[11338] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11339] Tan, J.; D'Agostaro, G. A. F.; Bendiak, B.; Reck, F.; Sarkar, M.; Squire, J. A.; Leong, P.; Schachter, H. : The human UDP-N-acetylglucosamine:alpha-6-D-mannoside-beta-1,2-N-acetylglucosaminyltransferase II gene (MGAT2): cloning of genomic DNA, localization to chromosome 14q21, expression in insect cells and purification of the recombinant protein. *Europ. J. Biochem.* 231: 317-328, 1995. ; and
- [11340] Yip, B.; Chen, S.-H.; Mulder, H.; Hoppener, J. W. M.; Schachter, H. : Organization of the human beta-1,2-N-acetylglucosaminyltransferase I gene (MGAT1), which controls complex and hybrid N-
- [11341] Further studies establishing the function and utilities of MGAT1 are found in John Hopkins OMIM database record ID 160995, and in cited publications numbered 3807-381 and 3817 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0182 (Accession XM_050495) is another VGAM165 host target gene. KIAA0182 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0182, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0182 BINDING SITE, designated SEQ ID:35643, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11342] Another function of VGAM165 is therefore inhibition of KIAA0182 (Accession XM_050495). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0182. KIAA1061 (Accession XM_048786) is another VGAM165 host target gene. KIAA1061 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1061, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1061 BINDING SITE, designated SEQ ID:35267, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11343] Another function of VGAM165 is therefore inhibition of KIAA1061 (Accession XM_048786). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1061. Phytanoyl-CoA Hydroxylase Interacting Protein (PHYHIP, Accession NM_014759) is another VGAM165 host target gene. PHYHIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PHYHIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHYHIP BINDING SITE, designated SEQ ID:16511, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11344] Another function of VGAM165 is therefore inhibition of Phytanoyl-CoA Hydroxylase Interacting Protein (PHYHIP, Accession NM_014759). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHYHIP.

STRAIT11499 (Accession NM_021242) is another VGAM165 host target gene. STRAIT11499 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STRAIT11499, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

STRAIT11499 BINDING SITE, designated SEQ ID:22211, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11345] Another function of VGAM165 is therefore inhibition of STRAIT11499 (Accession NM_021242). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRAIT11499. LOC157753 (Accession XM_088381) is another VGAM165 host target gene. LOC157753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157753 BINDING SITE, designated SEQ ID:39662, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11346] Another function of VGAM165 is therefore inhibition of LOC157753 (Accession XM_088381). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157753. LOC253070 (Accession XM_173088) is another VGAM165 host target gene. LOC253070 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253070 BINDING SITE, designated SEQ ID:46355, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11347] Another function of VGAM165 is therefore inhibition of LOC253070 (Accession XM_173088). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253070. LOC257479 (Accession XM_171548) is another VGAM165 host target gene. LOC257479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257479 BINDING SITE, designated SEQ ID:46050, to the nucleotide sequence of VGAM165 RNA, herein designated VGAM RNA, also designated SEQ ID:2876.

[11348] Another function of VGAM165 is therefore inhibition of

LOC257479 (Accession XM_171548). Accordingly, utilities of VGAM165 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257479. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 166 (VGAM166) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11349] VGAM166 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM166 was detected is described hereinabove with reference to Figs. 1–8.

[11350] VGAM166 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11351] VGAM166 gene encodes a VGAM166 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM166 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM166 precursor RNA is designated SEQ ID:152, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:152 is located at position 222866 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11352] VGAM166 precursor RNA folds onto itself, forming VGAM166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11353] An enzyme complex designated DICER COMPLEX, `dices` the VGAM166 folded precursor RNA into VGAM166 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM166 RNA is designated SEQ ID:2877, and is provided hereinbelow with reference to the sequence listing part.

[11354] VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM166 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11355] VGAM166 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM166 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM166 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11356] The complementary binding of VGAM166 RNA, herein designated VGAM RNA, to host target binding sites on VGAM166 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM166 host target RNA into VGAM166 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11357] It is appreciated that VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM166 host target genes. The mRNA of each one of this plurality of VGAM166 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM166 RNA, herein designated VGAM RNA, and which when bound by VGAM166 RNA causes inhibition of translation of respective one or more VGAM166 host target proteins.

[11358] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM166 gene, herein designated VGAM GENE, on one or more VGAM166 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11359] It is yet further appreciated that a function of VGAM166 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM166 correlate with, and may be deduced from, the identity of the host target genes which VGAM166 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11360] Nucleotide sequences of the VGAM166 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM166 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM166 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM166 are further described hereinbelow with reference to Table 1.

[11361] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM166 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM166 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[11362] As mentioned hereinabove with reference to Fig. 1, a function of VGAM166 gene, herein designated VGAM is inhibition of expression of VGAM166 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM166 correlate with, and may be deduced from, the identity of the target genes which VGAM166 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11363] Cholinergic Receptor, Nicotinic, Beta Polypeptide 2 (neuronal) (CHRNA2, Accession NM_000748) is a VGAM166 host target gene. CHRNA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRNA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRNA2 BINDING SITE, designated SEQ ID:6401, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11364] A function of VGAM166 is therefore inhibition of Cholinergic Receptor, Nicotinic, Beta Polypeptide 2 (neuronal)

(CHRNA2, Accession NM_000748), a gene which mediates fast signal transmission at synapses. Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRNA2. The function of CHRNA2 has been established by previous studies. The nicotinic acetylcholine receptors (OMIM Ref. No. nAChRs) are members of a superfamily of ligand-gated ion channels that mediate fast signal transmission at synapses. The nAChRs are thought to be (OMIM Ref. No. hetero)pentamers composed of homologous subunits. See 118508 for additional background information on nAChRs. In affected members of a Scottish family with type 3 nocturnal frontal lobe epilepsy (OMIM Ref. No. 605375), Phillips et al. (2001) identified a G-to-A transition at nucleotide 1025 in the CHRNA2 gene, resulting in a val287-to-met (V287M) substitution within the M2 domain. Codon 287 was also involved in the family reported by De Fusco et al. (2000); see 118507.0001. The mutation is located in an evolutionarily conserved region of the gene. Functional receptors with the V287M mutation were highly expressed in *Xenopus* oocytes and characterized by an approximately 10-fold increase in acetylcholine sensitivity. Animal model experiments lend further support to

the function of CHRNA2. Picciotto et al. (1995) disrupted the CHRNA2 mouse homolog in embryonic stem (ES) cells to generate 'knockout' mice deficient in this subunit. Homozygous mice were viable, mated normally, and showed no obvious physical deficits. However, their brains showed absence of high-affinity binding sites for nicotine, and electrophysiologic recordings from brain slices showed that thalamic neurons did not respond to nicotine application. Furthermore, behavioral tests demonstrated that nicotine no longer augmented the performance of the deficient mice on passive avoidance, a test of associative memory. Paradoxically, mutant mice were able to perform better than their nonmutant sibs on this task.

[11365] It is appreciated that the abovementioned animal model for CHRNA2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11366] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11367] Phillips, H. A.; Favre, I.; Kirkpatrick, M.; Zuberi, S. M.; Goudie, D.; Heron, S. E.; Scheffer, I. E.; Sutherland, G. R.; Berkovic, S. F.; Bertrand, D.; Mulley, J. C. : CHRNA2 is the

second acetylcholine receptor subunit associated with autosomal dominant nocturnal frontal lobe epilepsy. Am. J. Hum. Genet. 68: 225–231, 2001. ; and

- [11368] De Fusco, M.; Becchetti, A.; Patrignani, A.; Annesi, G.; Gambardella, A.; Quattrone, A.; Ballabio, A.; Wanke, E.; Casari, G. : The nicotinic receptor beta-2 subunit is mutant in nocturn.
- [11369] Further studies establishing the function and utilities of CHRNA2 are found in John Hopkins OMIM database record ID 118507, and in cited publications numbered 12690–4453, 12691, 390, 12692, 12693–12694, 39 and 12695 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM_030751) is another VGAM166 host target gene. TCF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF8 BINDING SITE, designated SEQ ID:25037, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2877.

[11370] Another function of VGAM166 is therefore inhibition of Transcription Factor 8 (represses interleukin 2 expression) (TCF8, Accession NM_030751), a gene which may be responsible for transcriptional repression of the il-2 gene and regulates the promoter activity of the atp1a1 gene . Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF8. The function of TCF8 has been established by previous studies. TCF8 encodes a human zinc finger transcription factor (Nil-2-a, negative regulator of IL2) that represses T-lymphocyte-specific interleukin-2 gene expression by interacting with a negative regulatory domain within the IL2 gene promoter/enhancer (Williams et al., 1991). Nil-2-a inhibits IL2 gene expression by binding to a negative regulatory domain 100 nucleotides 5-prime of the IL2 transcription start site. Williams et al. (1992) used Southern hybridization and somatic cell hybrids to demonstrate that the murine and human genomes contain homologous genes and that the TCF8 gene resides on human chromosome 10. Fluorescence in situ hybridization localized TCF8 to 10p11.2.

[11371] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [11372] Williams, T. M.; Montoya, G.; Wu, Y.; Eddy, R. L.; Byers, M. G.; Shows, T. B. : The TCF8 gene encoding a zinc finger protein (Nil-2-a) resides on human chromosome 10p11.2. Genomics 14: 194-196, 1992. ; and
- [11373] Williams, T. M.; Moolten, D.; Burlein, J.; Romano, J.; Bhaerman, R.; Godillot, A.; Mellon, M.; Rauscher, F. J., III; Kant, J. A. : Identification of a zinc finger protein that inhibits.
- [11374] Further studies establishing the function and utilities of TCF8 are found in John Hopkins OMIM database record ID 189909, and in cited publications numbered 1266 and 12683 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 20 Open Reading Frame 97 (C20orf97, Accession NM_021158) is another VGAM166 host target gene. C20orf97 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf97, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf97 BINDING SITE, designated SEQ ID:22138, to the nucleotide sequence of VGAM166

RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11375] Another function of VGAM166 is therefore inhibition of Chromosome 20 Open Reading Frame 97 (C20orf97, Accession NM_021158). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf97. DKFZp762E1511 (Accession XM_003460) is another VGAM166 host target gene. DKFZp762E1511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762E1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762E1511 BINDING SITE, designated SEQ ID:29936, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11376] Another function of VGAM166 is therefore inhibition of DKFZp762E1511 (Accession XM_003460). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762E1511. FLJ11618 (Accession NM_022452)

is another VGAM166 host target gene. FLJ11618 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ11618, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11618 BINDING SITE, designated SEQ ID:22791, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11377] Another function of VGAM166 is therefore inhibition of FLJ11618 (Accession NM_022452). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11618. FLJ14326 (Accession NM_032191) is another VGAM166 host target gene. FLJ14326 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14326, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14326 BINDING SITE, designated SEQ ID:25903, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11378] Another function of VGAM166 is therefore inhibition of FLJ14326 (Accession NM_032191). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14326. KIAA0863 (Accession XM_170863) is another VGAM166 host target gene. KIAA0863 BINDING SITE1 and KIAA0863 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0863, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0863 BINDING SITE1 and KIAA0863 BINDING SITE2, designated SEQ ID:45633 and SEQ ID:17153 respectively, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11379] Another function of VGAM166 is therefore inhibition of KIAA0863 (Accession XM_170863). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0863. KIAA1655 (Accession XM_039442) is another VGAM166 host target gene. KIAA1655 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1655, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1655 BINDING SITE, designated SEQ ID:33082, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11380] Another function of VGAM166 is therefore inhibition of KIAA1655 (Accession XM_039442). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1655. Olfactory Receptor, Family 7, Subfamily C, Member 1 (OR7C1, Accession NM_017506) is another VGAM166 host target gene. OR7C1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by OR7C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OR7C1 BINDING SITE, designated SEQ ID:18960, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11381] Another function of VGAM166 is therefore inhibition of Olfactory Receptor, Family 7, Subfamily C, Member 1

(OR7C1, Accession NM_017506). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OR7C1. SEC22C (Accession NM_004206) is another VGAM166 host target gene. SEC22C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC22C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC22C BINDING SITE, designated SEQ ID:10404, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11382] Another function of VGAM166 is therefore inhibition of SEC22C (Accession NM_004206). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC22C. ZFP106 (Accession NM_022473) is another VGAM166 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the

nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22835, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11383] Another function of VGAM166 is therefore inhibition of ZFP106 (Accession NM_022473). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC147043 (Accession XM_102732) is another VGAM166 host target gene. LOC147043 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147043, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147043 BINDING SITE, designated SEQ ID:42144, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11384] Another function of VGAM166 is therefore inhibition of LOC147043 (Accession XM_102732). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147043. LOC147229 (Accession XM_085742) is an-

other VGAM166 host target gene. LOC147229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147229 BINDING SITE, designated SEQ ID:38321, to the nucleotide sequence of VGAM166 RNA, herein designated VGAM RNA, also designated SEQ ID:2877.

[11385] Another function of VGAM166 is therefore inhibition of LOC147229 (Accession XM_085742). Accordingly, utilities of VGAM166 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147229. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 167 (VGAM167) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11386] VGAM167 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM167 was detected is described

hereinabove with reference to Figs. 1–8.

[11387] VGAM167 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11388] VGAM167 gene encodes a VGAM167 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM167 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM167 precursor RNA is designated SEQ ID:153, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:153 is located at position 169164 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11389] VGAM167 precursor RNA folds onto itself, forming VGAM167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11390] An enzyme complex designated DICER COMPLEX, `dices` the VGAM167 folded precursor RNA into VGAM167 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM167 RNA is designated SEQ ID:2878, and is provided hereinbelow with reference to the sequence listing part.

[11391] VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM167 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11392] VGAM167 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM167 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM167 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[11393] The complementary binding of VGAM167 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM167 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM167 host target RNA into VGAM167 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11394] It is appreciated that VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM167 host target genes. The mRNA of each one of this plurality of VGAM167 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM167 RNA, herein designated VGAM RNA, and which when bound by VGAM167 RNA causes inhibition of translation of respective one or more VGAM167 host target proteins.

[11395] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM167 gene, herein designated VGAM GENE, on one or more VGAM167 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11396] It is yet further appreciated that a function of VGAM167 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM167 correlate with, and may be deduced from, the identity of the host target genes which VGAM167 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11397] Nucleotide sequences of the VGAM167 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM167 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM167 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM167 are further described hereinbelow with reference to Table 1.

[11398] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM167 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM167 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11399] As mentioned hereinabove with reference to Fig. 1, a function of VGAM167 gene, herein designated VGAM is inhibition of expression of VGAM167 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM167 correlate with, and may be deduced from, the identity of the target genes which VGAM167 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11400] CD3Z Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Accession NM_000734) is a VGAM167 host target gene. CD3Z BINDING SITE is HOST TARGET binding site found in

the 3' untranslated region of mRNA encoded by CD3Z, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD3Z BINDING SITE, designated SEQ ID:6392, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11401] A function of VGAM167 is therefore inhibition of CD3Z Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Accession NM_000734), a gene which may involve in assembly and expression of the tcr complex as well as signal transduction upon antigen triggering. Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD3Z. The function of CD3Z has been established by previous studies. Alarcon et al. (1988) described 2 brothers who had a low expression of antigen receptor on the surface of their T lymphocytes. Functional analyses of their T cells showed impaired immune response to alloantigens, tetanus toxoid, and mitogens. Biochemical studies showed reduced intracellular expression of CD3-zeta chains; all other components of the T-cell receptor-CD3 complex were expressed normally. Alarcon et al. (1988) suggested that the

impaired association of the CD3–zeta chain with the other chains of the complex was the primary defect leading to the low expression of T–cell receptor–CD3 complex and immunodeficiency in these children. Failure to thrive had been diagnosed in the proband at 11 months; subsequently, chronic anorexia, diarrhea, and recurrent episodes of bronchopneumonia were noted. The diarrhea was shown to be associated with a malabsorption syndrome, which was unresponsive to a gluten–free diet. Biopsy of the small bowel showed absence of villi; however, the patient was negative for HLA–DR3 and –DR7. The boy died of severe autoimmune hemolytic anemia at the age of 3 years. The patient's brother had required hospital admission for respiratory infection, but on the whole was much more mildly affected than his brother. Animal model experiments lend further support to the function of CD3Z. Class I MHC molecules, known to be important for immune responses to antigen, are expressed also by neurons that undergo activity–dependent, long–term structural and synaptic modifications. Huh et al. (2000) showed that in mice genetically deficient for cell surface class I MHC, due to deletion of either TAP1 (OMIM Ref. No. 170260) or beta–2–microglobulin (OMIM Ref. No.

109700), or for the class I MHC receptor component CD3Z, refinement of connections between retina and central targets during development is incomplete. In the hippocampus of adult mutants, N-methyl-D-aspartate receptor-dependent long-term potentiation is enhanced, and long-term depression is absent. Specific class I MHC mRNAs are expressed by distinct mosaics of neurons, reflecting a potential for diverse neuronal functions. These results demonstrated an important role for these molecules in the activity-dependent remodeling and plasticity of connections in the developing and mature mammalian central nervous system.

[11402] It is appreciated that the abovementioned animal model for CD3Z is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11403] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11404] Huh, G. S.; Boulanger, L. M.; Du, H.; Riquelme, P. A.; Brotz, T. M.; Shatz, C. J. : Functional requirement for class I MHC in CNS development and plasticity. Science 290: 2155-2159, 2000. ; and

[11405] Alarcon, B.; Regueiro, J. R.; Arnaiz-Villena, A.; Terhorst, C. : Familial defect in the surface expression of the T-cell receptor-CD3 complex. New Eng. J. Med. 319: 1203-1208, 1988.

[11406] Further studies establishing the function and utilities of CD3Z are found in John Hopkins OMIM database record ID 186780, and in cited publications numbered 5687-5690, 1946, 569 and 10857-5694 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962) is another VGAM167 host target gene. IL22RA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL22RA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL22RA2 BINDING SITE, designated SEQ ID:27522, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11407] Another function of VGAM167 is therefore inhibition of Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962), a gene which induces the production of

acute-phase reactants. Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL22RA2. The function of IL22RA2 has been established by previous studies. IL22 (OMIM Ref. No. 605330), a homolog of IL10 (OMIM Ref. No. 124092), is secreted by T cells and binds to and signals through the class II cytokine receptor family (CRF) heterodimer IL22R (OMIM Ref. No. 605457)/IL10RB (OMIM Ref. No. 123889). IL22 induces the production of acute-phase reactants. By DNA database screening for sequences with homology to the extracellular domain of IL10RB and analysis of 6q24 BAC clone, Dumoutier et al. (2001) identified a cDNA encoding IL22BP, which they designated CRF2X. Sequence analysis predicted that the 231-amino acid protein, approximately 33% identical to the extracellular domains of IL20RA (OMIM Ref. No. 605620) and IL22R, contains a signal peptide, 4 cysteines conserved among members of the class II cytokine receptor family, and 5 potential N-linked glycosylation sites, but lacks a transmembrane domain. RT-PCR analysis detected expression in breast, lungs, and intestinal tract, with lower levels in skin, testis, brain, heart, and thymus. ELISA showed that IL22BP does indeed bind IL22. Func-

tional and luciferase reporter analysis indicated that IL22BP specifically blocked IL22-induced STAT3 (OMIM Ref. No. 102582) activation in an intestinal epithelial cell line. Using similar methods, Kotenko et al. (2001) also cloned and characterized IL22BP, which they initially designated CRF2-10. Western blot analysis showed expression of a 34- to 35-kD glycosylated secreted protein. Crosslinking and autoradiographic analysis confirmed the interaction of IL22 and IL22BP. Functional analysis indicated that IL22BP inhibited IL22-mediated MHC class I antigen expression. EMSA analysis demonstrated inhibition of STAT1 (OMIM Ref. No. 600555) and STAT3 DNA-binding complexes. Northern blot analysis showed blocking of SOCS3 (OMIM Ref. No. 604176) expression.

[11408] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11409] Dumoutier, L.; Lejeune, D.; Colau, D.; Renauld, J. C. : Cloning and characterization of IL-22 binding protein, a natural antagonist of IL-10-related T cell-derived inducible factor/IL 22. J. Immun. 166: 7090-7095, 2001. ; and

[11410] Kotenko, S. V.; Izotova, L. S.; Mirochnitchenko, O. V.; Es-

terova, E.; Dickensheets, H.; Donnelly, R. P.; Pestka, S. :
Identification, cloning, and characterization of a novel soluble re.

[11411] Further studies establishing the function and utilities of IL22RA2 are found in John Hopkins OMIM database record ID 606648, and in cited publications numbered 6128–6130 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM_002241) is another VGAM167 host target gene. KCNJ10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNJ10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ10 BINDING SITE, designated SEQ ID:8027, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11412] Another function of VGAM167 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 10 (KCNJ10, Accession NM_002241), a gene which may be responsible for potassium buffering action of glial

cells in the brain. Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ10. The function of KCNJ10 has been established by previous studies.

Potassium channels have been found in virtually all cells, and a large number of K(+) channel cDNAs have been cloned. They are generally classified into voltage-dependent (Kv) type (e.g., 176258 and 176264) and inwardly rectifying (Kir) type (e.g., 602106 and 600937). The former possesses 6 putative transmembrane regions, while the latter has 2 putative transmembrane regions. Doupnik et al. (1995) reported that Kir channels exhibit various physiologic functions, such as the maintenance of the resting membrane potential, the generation of prolonged action potentials, the modulation of cell excitability, and the transport of potassium ions. Takumi et al. (1995) reported that the K(AB)-2/Kir4.1 inwardly rectifying K(+) channel of rat has an ATP-binding domain of Walker-type A motif in the C-terminal intracellular region and is expressed in brain and kidney. In situ hybridization demonstrated that it is expressed predominantly in glial cells of rat membrane but also in the retinal Muller glial cells and marginal cells of the inner ear. By interspecific backcross

analysis, Tada et al. (1997) demonstrated that the mouse gene encoding the glial inwardly rectifying potassium channel, symbolized Kcnj10 by them, maps to distal chromosome 1. Because of homology of this region of the mouse genome to human 1q, Tada et al. (1997) suggested that the putative human homolog, KCNJ10, maps to 1q

[11413] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11414] Doupnik, C. A.; Davidson, N.; Lester, H. A. : The inward rectifier potassium channel family. Curr. Opin. Neurobiol. 5: 268–277, 1995. ; and

[11415] Tada, Y.; Horio, Y.; Takumi, T.; Terayama, M.; Tsuji, L.; Copeland, N. G.; Jenkins, N. A.; Kurachi, Y. : Assignment of the glial inwardly rectifying potassium channel K(AB)–2/Kir4.1 (Kcn.

[11416] Further studies establishing the function and utilities of KCNJ10 are found in John Hopkins OMIM database record ID 602208, and in cited publications numbered 8843–8845 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152) is another VGAM167 host target

gene. C20orf12 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf12 BINDING SITE, designated SEQ ID:19959, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11417] Another function of VGAM167 is therefore inhibition of Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152). Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf12.

KIAA0528 (Accession XM_051454) is another VGAM167 host target gene. KIAA0528 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0528 BINDING SITE, designated SEQ ID:35841, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2878.

[11418] Another function of VGAM167 is therefore inhibition of KIAA0528 (Accession XM_051454). Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0528. KIAA1493 (Accession XM_034415) is another VGAM167 host target gene. KIAA1493 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1493, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1493 BINDING SITE, designated SEQ ID:32089, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11419] Another function of VGAM167 is therefore inhibition of KIAA1493 (Accession XM_034415). Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1493. LOC51145 (Accession NM_016158) is another VGAM167 host target gene. LOC51145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51145, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51145 BINDING SITE, designated SEQ ID:18248, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11420] Another function of VGAM167 is therefore inhibition of LOC51145 (Accession NM_016158). Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51145. LOC92218 (Accession XM_043647) is another VGAM167 host target gene. LOC92218 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92218, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92218 BINDING SITE, designated SEQ ID:33985, to the nucleotide sequence of VGAM167 RNA, herein designated VGAM RNA, also designated SEQ ID:2878.

[11421] Another function of VGAM167 is therefore inhibition of LOC92218 (Accession XM_043647). Accordingly, utilities of VGAM167 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC92218. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 168 (VGAM168) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11422] VGAM168 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM168 was detected is described hereinabove with reference to Figs. 1–8.

[11423] VGAM168 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11424] VGAM168 gene encodes a VGAM168 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM168 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM168 precursor RNA is designated SEQ

ID:154, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:154 is located at position 286571 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11425] VGAM168 precursor RNA folds onto itself, forming VGAM168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11426] An enzyme complex designated DICER COMPLEX, `dices` the VGAM168 folded precursor RNA into VGAM168 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM168 RNA is designated SEQ ID:2879, and

is provided hereinbelow with reference to the sequence listing part.

[11427] VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM168 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11428] VGAM168 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM168 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM168 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11429] The complementary binding of VGAM168 RNA, herein designated VGAM RNA, to host target binding sites on VGAM168 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM168 host target RNA into VGAM168 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11430] It is appreciated that VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM168 host target genes. The mRNA of each one of this plurality of VGAM168 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM168 RNA, herein designated VGAM RNA, and which when bound by VGAM168 RNA causes inhibition of translation of respective one or more VGAM168 host target proteins.

[11431] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM168 gene, herein designated VGAM GENE, on one or more VGAM168 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11432] It is yet further appreciated that a function of VGAM168 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM168 correlate with, and may be deduced from, the identity of the host target genes which VGAM168 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11433] Nucleotide sequences of the VGAM168 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM168 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM168 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM168 are further described hereinbelow with reference to Table 1.

[11434] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM168 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM168 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11435] As mentioned hereinabove with reference to Fig. 1, a function of VGAM168 gene, herein designated VGAM is inhibition of expression of VGAM168 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM168 correlate with, and may be deduced from, the identity of the target genes which VGAM168 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11436] RAS, Dexamethasone-induced 1 (RASD1, Accession NM_016084) is a VGAM168 host target gene. RASD1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASD1 BINDING SITE, designated SEQ ID:18167, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11437] A function of VGAM168 is therefore inhibition of RAS, Dexamethasone-induced 1 (RASD1, Accession NM_016084), a gene which is a novel physiologic NO effector. Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with RASD1. The function of RASD1 has been established by previous studies. Using differential display, Kemppainen and Behrend (1998) identified Dexras1, a novel RAS superfamily gene induced by dexamethasone in AtT-20 cells (mouse-derived corticotroph tumor cells). The deduced 280-amino acid mouse protein shares highest homology (36% identity) with human RAP2B (OMIM Ref. No. 179541). Northern blot analysis of mouse tissues detected expression of Dexras1 in brain, heart, kidney, and liver. By yeast 2-hybrid screening of a lung cDNA library with the third SH3 domain of NCK2 (OMIM Ref. No. 604930) as bait, Tu and Wu (1999) isolated a cDNA encoding RASD1, which they called DEXRAS1. The deduced 281-amino acid protein, which is 98% identical to the mouse protein, contains a P loop, guanine base-binding loops, and a C-terminal farnesylation site. SDS-PAGE analysis detected a 33-kD protein, close to the predicted size. Northern blot analysis revealed ubiquitous expression of a 5.0-kb RASD1 transcript, with highest levels in heart. Dexamethasone exposure upregulated RASD1 expression.

[11438] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [11439] Kemppainen, R. J.; Behrend, E. N. : Dexamethasone rapidly induces a novel Ras superfamily member-related gene in AtT-20 cells. *J. Biol. Chem.* 273: 3129-3131, 1998. ; and
- [11440] Tu, Y.; Wu, C. : Cloning, expression and characterization of a novel human Ras-related protein that is regulated by glucocorticoid hormone. *Biochim. Biophys. Acta* 1489: 452-456, 1999.
- [11441] Further studies establishing the function and utilities of RASD1 are found in John Hopkins OMIM database record ID 605550, and in cited publications numbered 6402-6404 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine Racemase (SRR, Accession NM_021947) is another VGAM168 host target gene. SRR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRR BINDING SITE, designated SEQ ID:22474, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11442] Another function of VGAM168 is therefore inhibition of Serine Racemase (SRR, Accession NM_021947). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRR. DKFZp762E1511 (Accession XM_003460) is another VGAM168 host target gene. DKFZp762E1511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762E1511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762E1511 BINDING SITE, designated SEQ ID:29933, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11443] Another function of VGAM168 is therefore inhibition of DKFZp762E1511 (Accession XM_003460). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp762E1511. SDS3 (Accession XM_045014) is another VGAM168 host target gene. SDS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDS3, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDS3 BINDING SITE, designated SEQ ID:34318, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11444] Another function of VGAM168 is therefore inhibition of SDS3 (Accession XM_045014). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDS3. LOC151248 (Accession XM_087143) is another VGAM168 host target gene. LOC151248 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151248 BINDING SITE, designated SEQ ID:39086, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11445] Another function of VGAM168 is therefore inhibition of LOC151248 (Accession XM_087143). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC151248. LOC153810 (Accession XM_087778) is another VGAM168 host target gene. LOC153810 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153810, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153810 BINDING SITE, designated SEQ ID:39412, to the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11446] Another function of VGAM168 is therefore inhibition of LOC153810 (Accession XM_087778). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153810. LOC170425 (Accession XM_084330) is another VGAM168 host target gene. LOC170425 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC170425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170425 BINDING SITE, designated SEQ ID:37551, to

the nucleotide sequence of VGAM168 RNA, herein designated VGAM RNA, also designated SEQ ID:2879.

[11447] Another function of VGAM168 is therefore inhibition of LOC170425 (Accession XM_084330). Accordingly, utilities of VGAM168 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170425. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 169 (VGAM169) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11448] VGAM169 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM169 was detected is described hereinabove with reference to Figs. 1–8.

[11449] VGAM169 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11450] VGAM169 gene encodes a VGAM169 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM169 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM169 precursor RNA is designated SEQ ID:155, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:155 is located at position 40241 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11451] VGAM169 precursor RNA folds onto itself, forming VGAM169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11452] An enzyme complex designated DICER COMPLEX, `dices` the VGAM169 folded precursor RNA into VGAM169 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM169 RNA is designated SEQ ID:2880, and is provided hereinbelow with reference to the sequence listing part.

[11453] VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM169 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11454] VGAM169 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM169 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM169 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11455] The complementary binding of VGAM169 RNA, herein designated VGAM RNA, to host target binding sites on VGAM169 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM169 host target RNA into VGAM169 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11456] It is appreciated that VGAM169 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM169 host target genes. The mRNA of each one of this plurality of VGAM169 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM169 RNA, herein designated VGAM RNA, and which when bound by VGAM169 RNA causes inhibition of translation of respective one or more VGAM169 host target proteins.

[11457] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM169 gene, herein designated VGAM GENE, on one or more VGAM169 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[11458] It is yet further appreciated that a function of VGAM169 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM169 correlate with, and may be deduced from, the identity of the host target genes which VGAM169 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11459] Nucleotide sequences of the VGAM169 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM169 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM169 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM169 are further described hereinbelow with reference to Table 1.

[11460] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM169 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM169 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11461] As mentioned hereinabove with reference to Fig. 1, a function of VGAM169 gene, herein designated VGAM is inhibition of expression of VGAM169 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM169 correlate with, and may be deduced from, the identity of the target genes which VGAM169 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11462] Astrotactin (ASTN, Accession XM_045113) is a VGAM169 host target gene. ASTN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ASTN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ASTN BINDING SITE, designated SEQ ID:34361, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11463] A function of VGAM169 is therefore inhibition of Astro-tactin (ASTN, Accession XM_045113). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ASTN. Calpain 2, (m/II) Large Subunit (CAPN2, Accession NM_001748) is another VGAM169 host target gene. CAPN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN2 BINDING SITE, designated SEQ ID:7485, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11464] Another function of VGAM169 is therefore inhibition of Calpain 2, (m/II) Large Subunit (CAPN2, Accession NM_001748). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN2. Fanconi Anemia, Complementation Group F (FANCF, Accession NM_022725) is another VGAM169 host target gene. FANCF BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by FANCF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FANCF BINDING SITE, designated SEQ ID:22922, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11465] Another function of VGAM169 is therefore inhibition of Fanconi Anemia, Complementation Group F (FANCF, Accession NM_022725). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FANCF. Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM_080821) is another VGAM169 host target gene. C20orf108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf108, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf108 BINDING SITE, designated SEQ ID:28087, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ

ID:2880.

[11466] Another function of VGAM169 is therefore inhibition of Chromosome 20 Open Reading Frame 108 (C20orf108, Accession NM_080821). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf108. Cyclin G2 (CCNG2, Accession NM_004354) is another VGAM169 host target gene. CCNG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCNG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNG2 BINDING SITE, designated SEQ ID:10560, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11467] Another function of VGAM169 is therefore inhibition of Cyclin G2 (CCNG2, Accession NM_004354). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNG2. CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM_006035) is another VGAM169 host target gene. CDC42BPB BINDING SITE

is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDC42BPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC42BPB BINDING SITE, designated SEQ ID:12657, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11468] Another function of VGAM169 is therefore inhibition of CDC42 Binding Protein Kinase Beta (DMPK-like) (CDC42BPB, Accession NM_006035). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC42BPB. KIAA0210 (Accession NM_014744) is another VGAM169 host target gene. KIAA0210 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0210, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0210 BINDING SITE, designated SEQ ID:16425, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11469] Another function of VGAM169 is therefore inhibition of KIAA0210 (Accession NM_014744). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0210. KIAA1486 (Accession XM_041126) is another VGAM169 host target gene. KIAA1486 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1486 BINDING SITE, designated SEQ ID:33460, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11470] Another function of VGAM169 is therefore inhibition of KIAA1486 (Accession XM_041126). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1486. LOC146823 (Accession XM_097105) is another VGAM169 host target gene. LOC146823 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC146823, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146823 BINDING SITE, designated SEQ ID:40748, to the nucleotide sequence of VGAM169 RNA, herein designated VGAM RNA, also designated SEQ ID:2880.

[11471] Another function of VGAM169 is therefore inhibition of LOC146823 (Accession XM_097105). Accordingly, utilities of VGAM169 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146823. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 170 (VGAM170) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11472] VGAM170 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM170 was detected is described hereinabove with reference to Figs. 1–8.

[11473] VGAM170 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM170 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11474] VGAM170 gene encodes a VGAM170 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM170 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM170 precursor RNA is designated SEQ ID:156, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:156 is located at position 152649 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11475] VGAM170 precursor RNA folds onto itself, forming VGAM170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11476] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM170 folded precursor RNA into VGAM170 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM170 RNA is designated SEQ ID:2881, and is provided hereinbelow with reference to the sequence listing part.

[11477] VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM170 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11478] VGAM170 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM170 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM170 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11479] The complementary binding of VGAM170 RNA, herein designated VGAM RNA, to host target binding sites on VGAM170 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM170 host target RNA into VGAM170 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11480] It is appreciated that VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM170 host target genes. The mRNA of each one of this plurality of VGAM170 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM170 RNA, herein designated VGAM RNA, and which when bound by VGAM170 RNA causes inhibition of translation of respective one or more VGAM170 host target proteins.

[11481] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM170 gene, herein designated VGAM GENE, on one or more VGAM170 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11482] It is yet further appreciated that a function of VGAM170 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM170 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM170 correlate with, and may be deduced from, the identity of the host target genes which VGAM170 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11483] Nucleotide sequences of the VGAM170 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM170 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM170 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM170 are further

described hereinbelow with reference to Table 1.

[11484] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM170 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM170 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11485] As mentioned hereinabove with reference to Fig. 1, a function of VGAM170 gene, herein designated VGAM is inhibition of expression of VGAM170 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM170 correlate with, and may be deduced from, the identity of the target genes which VGAM170 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11486] Inhibitor of Growth Family, Member 1 (ING1, Accession NM_005537) is a VGAM170 host target gene. ING1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ING1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ING1

BINDING SITE, designated SEQ ID:12062, to the nucleotide sequence of VGAM170 RNA, herein designated VGAM RNA, also designated SEQ ID:2881.

[11487] A function of VGAM170 is therefore inhibition of Inhibitor of Growth Family, Member 1 (ING1, Accession NM_005537), a gene which acts as a potent growth regulator in normal and in established cells. Accordingly, utilities of VGAM170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ING1. The function of ING1 has been established by previous studies. Garkavtsev et al. (1996) described a new strategy for the isolation of tumor suppressor genes. This strategy was based on subtractive hybridization followed by selection of transforming genetic suppressor elements. It was used to isolate a novel gene called ING1 which encodes a 33-kD protein (294 amino acids) that displays the characteristics of a tumor suppressor gene. Garkavtsev et al. (1996) reported that expression of high levels of transfected constructs of this gene inhibited growth, while chronic expression of antisense constructs promoted cell transformation. They observed reduced expression of ING1 in some breast cancer cell lines and mutation of ING1 in neuroblastoma cells. Garkavtsev et al. (1997)

showed, using indirect immunofluorescence, that the p33(ING1) protein is located in the nucleus, which is consistent with its proposed role as a growth regulator. By fluorescence in situ hybridization, they localized the ING1 gene to 13q33–q34. Using the radiation hybrid mapping technique, Zeremski et al. (1997) mapped ING1 to 13q34.

[11488] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11489] Garkavtsev, I.; Kazarov, A.; Gudkov, A.; Riabowol, K. : Suppression of the novel growth inhibitor p33(ING1) promotes neoplastic transformation. *Nature Genet.* 14: 415–420, 1996. Note: Erratum: *Nature Genet.* 23: 373 only, 1999. ; and

[11490] Gunduz, M.; Ouchida, M.; Fukushima, K.; Hanafusa, H.; Etani, T.; Nishioka, S.; Nishizaki, K.; Shimizu, K. : Genomic structure of the human ING1 gene and tumor-specific mutations detected.

[11491] Further studies establishing the function and utilities of ING1 are found in John Hopkins OMIM database record ID 601566, and in cited publications numbered 2787–278 and 6496–2790 listed in the bibliography section herein–below, which are also hereby incorporated by refer–

ence.FLJ12476 (Accession NM_022784) is another VGAM170 host target gene. FLJ12476 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12476 BINDING SITE, designated SEQ ID:23069, to the nucleotide sequence of VGAM170 RNA, herein designated VGAM RNA, also designated SEQ ID:2881.

[11492] Another function of VGAM170 is therefore inhibition of FLJ12476 (Accession NM_022784). Accordingly, utilities of VGAM170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12476. KIAA1715 (Accession XM_042834) is another VGAM170 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33787, to the nucleotide sequence of VGAM170 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2881.

[11493] Another function of VGAM170 is therefore inhibition of KIAA1715 (Accession XM_042834). Accordingly, utilities of VGAM170 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 171 (VGAM171) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11494] VGAM171 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM171 was detected is described hereinabove with reference to Figs. 1–8.

[11495] VGAM171 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11496] VGAM171 gene encodes a VGAM171 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM171 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM171 precursor RNA is designated SEQ ID:157, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:157 is located at position 113416 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11497] VGAM171 precursor RNA folds onto itself, forming VGAM171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11498] An enzyme complex designated DICER COMPLEX, `dices` the VGAM171 folded precursor RNA into VGAM171 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM171 RNA is designated SEQ ID:2882, and is provided hereinbelow with reference to the sequence listing part.

[11499] VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM171 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11500] VGAM171 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM171 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM171 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11501] The complementary binding of VGAM171 RNA, herein designated VGAM RNA, to host target binding sites on VGAM171 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM171 host target RNA into VGAM171 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11502] It is appreciated that VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM171 host target genes. The mRNA of each one of this plurality of VGAM171 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM171 RNA, herein designated VGAM RNA, and which when bound by VGAM171 RNA causes inhibition of translation of respective one or more VGAM171 host target proteins.

[11503] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM171 gene, herein designated VGAM GENE, on one or more VGAM171 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[11504] It is yet further appreciated that a function of VGAM171 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM171 correlate with, and may be deduced from, the identity of the host target genes which VGAM171 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11505] Nucleotide sequences of the VGAM171 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM171 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM171 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM171 are further described hereinbelow with reference to Table 1.

[11506] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM171 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM171 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11507] As mentioned hereinabove with reference to Fig. 1, a function of VGAM171 gene, herein designated VGAM is inhibition of expression of VGAM171 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM171 correlate with, and may be deduced from, the identity of the target genes which VGAM171 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11508] ARP1 Actin-related Protein 1 Homolog B, Centractin Beta (yeast) (ACTR1B, Accession XM_047780) is a VGAM171 host target gene. ACTR1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTR1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1B BINDING SITE, designated SEQ ID:35053, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11509] A function of VGAM171 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog B, Centractin Beta (yeast) (ACTR1B, Accession XM_047780), a gene which component of a multi-subunit complex involved in microtubule based vesicle motility. Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACTR1B. The function of ACTR1B has been established by previous studies. Isoforms of actin (e.g., ACTG1; 102560), in association with myosin motor proteins (e.g., MYO1A; 601478), are required for cellular motile processes. In addition to conventional actins, there are several actin-related proteins (e.g., ACTR2; 604221). By searching an EST database and by screening a testis cDNA library, Clark et al. (1994) isolated cDNAs encoding ACTR1B, which they called beta-centractin. The deduced 376-amino acid ACTR1B protein and the ACTR1A protein (OMIM Ref. No. 605143) are of equal length, and they share 90% amino acid identity and 96% amino acid similarity. Northern blot analysis detected a 2.0-kb ACTR1B transcript at variable levels in all tissues tested. Two-dimensional immunoblot analysis determined that ACTR1B is expressed in the cytosol as part of the dynactin complex, an activator of dynein-driven vesicle

movement (see OMIM Ref. No. 601143), as a 43-kD protein with a pI of 6.4; levels of ACTR1B were at least 15-fold lower than those of ACTR1A. By somatic cell hybrid analysis, Elsea et al. (1999) mapped the ACTR1B gene to chromosome 2. They localized the ACTR1B gene to 2q11.1–q11.2 using FISH.

[11510] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11511] Clark, S. W.; Staub, O.; Clark, I. B.; Holzbaur, E. L. F.; Paschal, B. M.; Vallee, R. B.; Meyer, D. I. : Beta-centractin: characterization and distribution of a new member of the centractin family of actin-related proteins. *Molec. Biol. Cell* 5: 1301–1310, 1994. ; and

[11512] Elsea, S. H.; Clark, I. B.; Juyal, R. C.; Meyer, D. J.; Meyer, D. I.; Patel, P. I. : Assignment of beta-centractin (CTRN2) to human chromosome 2 bands q11.1–q11.2 with somatic cell hybr.

[11513] Further studies establishing the function and utilities of ACTR1B are found in John Hopkins OMIM database record ID 605144, and in cited publications numbered 2875–2876 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence.Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093) is another VGAM171 host target gene. CBFA2T2 BINDING SITE1 and CBFA2T2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBFA2T2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBFA2T2 BINDING SITE1 and CBFA2T2 BINDING SITE2, designated SEQ ID:11555 and SEQ ID:11550 respectively, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11514] Another function of VGAM171 is therefore inhibition of Core-binding Factor, Runt Domain, Alpha Subunit 2; Translocated To, 2 (CBFA2T2, Accession NM_005093), a gene which is a putative transcription factor. Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBFA2T2. The function of CBFA2T2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.POU Domain, Class 2,

Associating Factor 1 (POU2AF1, Accession NM_006235) is another VGAM171 host target gene. POU2AF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU2AF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU2AF1 BINDING SITE, designated SEQ ID:12895, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11515] Another function of VGAM171 is therefore inhibition of POU Domain, Class 2, Associating Factor 1 (POU2AF1, Accession NM_006235), a gene which is a transcriptional coactivator that specifically associates with either oct1 or oct2. Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU2AF1. The function of POU2AF1 has been established by previous studies. POU domain proteins contain a bipartite DNA-binding domain divided by a flexible linker that enables them to adopt various monomer configurations on DNA. The versatility of POU protein operation is additionally conferred at the dimerization level. Tomilin et al. (2000) found that the POU

dimer from the OCT1 gene formed on the palindromic OCT factor recognition element, or PORE (ATTTGAAATGCAAAT), could recruit the transcriptional coactivator OBF1, whereas POU dimers formed on the consensus MORE (more PORE) (ATGCATATGCAT) or on MOREs from Ig heavy chain promoters (AT[G/A][C/A]ATATGCAA) failed to interact. An interaction with OBF1 was precluded since the same OCT1 residues that form the MORE dimerization interface are also used for OBF1/OCT1 interactions on the PORE. These findings provided a paradigm of how specific POU dimer assemblies can differentially recruit a coregulatory activity with distinct transcriptional readouts. Animal model experiments lend further support to the function of POU2AF1. Schubart et al. (2001) noted that Oct2-deficient mice die at birth but have normal B-cell development and transcription of Ig genes. Obf1-deficient mice are viable with unaffected B-cell development in bone marrow and normal serum IgM but have reduced B-cell numbers in spleen and low serum IgG. By creating double knockout mice, Schubart et al. (2001) confirmed that B-cell development and Ig gene transcription can proceed normally without these B-cell specific factors. However, in these animals

the mature B-cell pool was strongly reduced, suggesting that these factors play an important role in controlling the expansion and/or maintenance of mature B cells.

[11516] It is appreciated that the abovementioned animal model for POU2AF1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11517] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11518] Schubart, K.; Massa, S.; Schubart, D.; Corcoran, L. M.; Rolink, A. G.; Matthias, P. : B cell development and immunoglobulin gene transcription in the absence of Oct-2 and OBF-1. *Nature Immun.* 2: 69-74, 2001. ; and

[11519] Tomilin, A.; Remenyi, A.; Lins, K.; Bak, H.; Leidel, S.; Vriend, G.; Wilmanns, M.; Scholer, H. R. : Synergism with the coactivator OBF-1 (OCA-B, BOB-1) is mediated by a specific POU dimer.

[11520] Further studies establishing the function and utilities of POU2AF1 are found in John Hopkins OMIM database record ID 601206, and in cited publications numbered 6375-6377, 6882, 10799-688 and 10797 listed in the bibliography section hereinbelow, which are also hereby

incorporated by reference. KIAA1950 (Accession XM_166532) is another VGAM171 host target gene. KIAA1950 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1950 BINDING SITE, designated SEQ ID:44492, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11521] Another function of VGAM171 is therefore inhibition of KIAA1950 (Accession XM_166532). Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1950. MGC2647 (Accession XM_057150) is another VGAM171 host target gene. MGC2647 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2647, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2647 BINDING SITE, designated SEQ ID:36485, to the nucleotide

sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11522] Another function of VGAM171 is therefore inhibition of MGC2647 (Accession XM_057150). Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2647. RTC Domain Containing 1 (RTCD1, Accession NM_003729) is another VGAM171 host target gene. RTCD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RTCD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RTCD1 BINDING SITE, designated SEQ ID:9822, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11523] Another function of VGAM171 is therefore inhibition of RTC Domain Containing 1 (RTCD1, Accession NM_003729). Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTCD1. SCMH1 (Accession NM_012236) is another VGAM171 host target gene.

SCMH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCMH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCMH1 BINDING SITE, designated SEQ ID:14540, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ ID:2882.

[11524] Another function of VGAM171 is therefore inhibition of SCMH1 (Accession NM_012236). Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCMH1. Tripartite Motif-containing 22 (TRIM22, Accession NM_006074) is another VGAM171 host target gene. TRIM22 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM22 BINDING SITE, designated SEQ ID:12718, to the nucleotide sequence of VGAM171 RNA, herein designated VGAM RNA, also designated SEQ

ID:2882.

- [11525] Another function of VGAM171 is therefore inhibition of Tripartite Motif-containing 22 (TRIM22, Accession NM_006074). Accordingly, utilities of VGAM171 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM22. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 172 (VGAM172) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [11526] VGAM172 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM172 was detected is described hereinabove with reference to Figs. 1–8.
- [11527] VGAM172 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [11528] VGAM172 gene encodes a VGAM172 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM172 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM172 precursor RNA is designated SEQ ID:158, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:158 is located at position 101644 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11529] VGAM172 precursor RNA folds onto itself, forming VGAM172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11530] An enzyme complex designated DICER COMPLEX, `dices` the VGAM172 folded precursor RNA into VGAM172 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM172 RNA is designated SEQ ID:2883, and is provided hereinbelow with reference to the sequence listing part.

[11531] VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM172 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11532] VGAM172 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM172 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM172 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11533] The complementary binding of VGAM172 RNA, herein designated VGAM RNA, to host target binding sites on VGAM172 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM172 host target RNA into VGAM172 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11534] It is appreciated that VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM172 host target genes. The mRNA of each one of this plurality of VGAM172 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM172 RNA, herein designated VGAM RNA, and which when bound by VGAM172 RNA causes inhibition of translation of respective one or more VGAM172 host target proteins.

[11535] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM172 gene, herein designated VGAM GENE, on one or more VGAM172 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[11536] It is yet further appreciated that a function of VGAM172 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM172 correlate with, and may be deduced from, the identity of the host target genes which VGAM172 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11537] Nucleotide sequences of the VGAM172 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM172 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM172 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM172 are further described hereinbelow with reference to Table 1.

[11538] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM172 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM172 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11539] As mentioned hereinabove with reference to Fig. 1, a function of VGAM172 gene, herein designated VGAM is inhibition of expression of VGAM172 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM172 correlate with, and may be deduced from, the identity of the target genes which VGAM172 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11540] Alpha-1-B Glycoprotein (A1BG, Accession NM_130786) is a VGAM172 host target gene. A1BG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by A1BG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A1BG BINDING SITE, designated SEQ ID:28277, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11541] A function of VGAM172 is therefore inhibition of Alpha-

1-B Glycoprotein (A1BG, Accession NM_130786), a gene which a plasma protein of unknown function. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A1BG. The function of A1BG has been established by previous studies. The complete amino acid sequence of alpha-1B-glycoprotein, a plasma protein of unknown function, was determined by Ishioka et al. (1986). Sequence homology to immunoglobulins was recognized. Alpha-1B-glycoprotein is present in normal adult plasma at an average concentration of 22 mg/dl. Gahne et al. (1987) observed genetic polymorphism of A1B using one-dimensional horizontal polyacrylamide gel electrophoresis followed by Western blotting with specific antiserum. Three different phenotypes, designated 1-1, 1-2, and 2-2, were observed. Family data supported the hypothesis that the three phenotypes are determined by 2 codominant alleles at an autosomal locus. In pigs the homologous locus is linked to malignant hyperthermia (OMIM Ref. No. 145600). Several other linkages in pigs and in horses suggest that human chromosomes 19, 6, and 1 are 'candidate chromosomes' for bearing the human A1B. Juneja et al. (1988) found a higher degree of A1B polymorphism in

American blacks than in Caucasian populations. They described new alleles. Eiberg et al. (1989) reported exclusion data for localization of the alpha-1B-glycoprotein gene polymorphism. Eiberg et al. (1989) found linkage between A1BG and Lutheran blood group (OMIM Ref. No. 111150); lod = 3.06 at theta = 0.05 in males, and lod = 1.42 at theta = 0.10 in females. They suggested that the most likely order of genes on chromosome 19 is C3--SE--LU--A1BG.

[11542] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11543] Ishioka, N.; Takahashi, N.; Putnam, F. W. : Amino acid sequence of human plasma alpha-1B-glycoprotein: homology to the immunoglobulin supergene family. Proc. Nat. Acad. Sci. 83: 2363-2367, 1986. ; and

[11544] Eiberg, H.; Bisgaard, M. L.; Mohr, J. : Linkage between alpha-1-B-glycoprotein (A1BG) and Lutheran (LU) red blood group system: assignment to chromosome 19: new genetic variants of A1BG.

[11545] Further studies establishing the function and utilities of A1BG are found in John Hopkins OMIM database record ID 138670, and in cited publications numbered

12027–12031 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Aconitase 1, Soluble (ACO1, Accession NM_002197) is another VGAM172 host target gene. ACO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACO1 BINDING SITE, designated SEQ ID:7955, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11546] Another function of VGAM172 is therefore inhibition of Aconitase 1, Soluble (ACO1, Accession NM_002197), a gene which an iron-dependent enzyme; catalyzes conversion of citrate to cis-aconitate in the TCA cycle. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACO1. The function of ACO1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53. A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM_007203) is another VGAM172

host target gene. AKAP2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AKAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP2 BINDING SITE, designated SEQ ID:14065, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11547] Another function of VGAM172 is therefore inhibition of A Kinase (PRKA) Anchor Protein 2 (AKAP2, Accession NM_007203), a gene which binds to regulatory subunit (rii) of protein kinase a. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP2. The function of AKAP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM18.Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082) is another VGAM172 host target gene. CKN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CKN1, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKN1 BINDING SITE, designated SEQ ID:5534, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11548] Another function of VGAM172 is therefore inhibition of Cockayne Syndrome 1 (classical) (CKN1, Accession NM_000082). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKN1. Fatty-acid-Coenzyme A Ligase, Long-chain 2 (FACL2, Accession NM_021122) is another VGAM172 host target gene. FACL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FACL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL2 BINDING SITE, designated SEQ ID:22097, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11549] Another function of VGAM172 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 2 (FACL2, Ac-

cession NM_021122), a gene which activates long-chain fatty acids for both synthesis of cellular lipids. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FACL2. The function of FACL2 has been established by previous studies. See 152425. Minoshima et al. (1991) isolated a human cDNA for a long-chain acyl-CoA synthetase from a human liver cDNA library using the rat cDNA as a probe. Using flow-sorted human chromosomes, they demonstrated that the gene, now designated FACL2, is located on human chromosome 4. Cantu et al. (1995) mapped FACL2 to 4q34-q35 by fluorescence in situ hybridization.

[11550] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11551] Cantu, E. S.; Sprinkle, T. J.; Ghosh, B.; Singh, I. : The human palmitoyl-CoA ligase (FACL2) gene maps to the chromosome 4q34-q35 region by fluorescence in situ hybridization (FISH) and somatic cell hybrid panels. *Genomics* 28: 600-602, 1995. ; and

[11552] Minoshima, S.; Fukuyama, R.; Yamamoto, T.; Shimizu, N. : Mapping of human long-chain acyl-CoA synthetase to

chromosome 4. (Abstract) Cytogenet. Cell Genet. 58: 1888 only, 1991.

[11553] Further studies establishing the function and utilities of FACL2 are found in John Hopkins OMIM database record ID 152426, and in cited publications numbered 3434 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Four and A Half LIM Domains 2 (FHL2, Accession NM_001450) is another VGAM172 host target gene. FHL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FHL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHL2 BINDING SITE, designated SEQ ID:7182, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11554] Another function of VGAM172 is therefore inhibition of Four and A Half LIM Domains 2 (FHL2, Accession NM_001450), a gene which Contains four LIM domains and an additional zinc finger. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHL2. The

function of FHL2 has been established by previous studies. LIM proteins contain a highly conserved double zinc finger motif called the LIM domain. By searching sequence databases with a partial human SLIM1 (FHL1; 300163) cDNA, Morgan and Madgwick (1996) identified partial SLIM3 cDNAs. Genini et al. (1997) used subtractive cloning to isolate a gene that is downregulated during transformation of normal myoblasts to rhabdomyosarcoma cells. The gene, termed DRAL for 'down-regulated in rhabdomyosarcoma LIM protein,' encodes a 279-amino acid polypeptide with an observed mass of 32 kD. The protein sequence contains 4 complete LIM domains and the second half of a fifth LIM domain. DRAL appears to be a member of the LIM-only class of proteins, which consist primarily of LIM domains and little else. Southern blotting revealed a single-copy gene that is conserved among vertebrates. Northern blotting revealed that the DRAL gene is expressed at highest levels in heart and ovary, and at lower levels in skeletal muscle, prostate, testis, small intestine, and colon. Results of Northern blotting of tumor cell lines suggested to Genini et al. (1997) that this gene may be downregulated during transformation of a variety of cell types. Genini et al. (1997) used in situ hybridization

to map the human FHL2 gene to 2q12–q14. By fluorescence in situ hybridization, Chan et al. (1998) mapped the FHL2 gene to 2q12–q13. Using the yeast 2–hybrid system, Tanahashi and Tabira (2000) screened for proteins interacting with an Alzheimer disease gene, presenilin–2 (OMIM Ref. No. 600759), and cloned DRAL. DRAL interacted with a hydrophilic loop region (amino acids 269–298) in the endoproteolytic N–terminal fragment of PS2, but not that of PS1 (OMIM Ref. No. 104311), although residues 269 to 298 of PS2 and the corresponding PS1 sequence differ by only 3 amino acids. Each of 9 PS2 point mutations within a region from residues 275 to 296 abolished the binding. The in vitro interaction was confirmed by affinity column assay and the physiologic interactions between endogenous PS2 and DRAL by coimmunoprecipitation from human lung fibroblast MRC5 cells. The authors suggested that DRAL functions as a link between PS2 and an intracellular signaling pathway.

[11555] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11556] Genini, M.; Schwalbe, P.; Scholl, F. A.; Remppis, A.; Mattei, M.–G.; Schafer, B. W. : Subtractive cloning and characteri–

zation of DRAL, a novel LIM-domain protein down-regulated in rhabdomyosarcoma. DNA Cell Biol. 16: 433-442, 1997. ; and

[11557] Tanahashi, H.; Tabira, T. : Alzheimer's disease-associated presenilin 2 interacts with DRAL, an LIM-domain protein. Hum. Molec. Genet. 9: 2281-2289, 2000.

[11558] Further studies establishing the function and utilities of FHL2 are found in John Hopkins OMIM database record ID 602633, and in cited publications numbered 8751-875 and 11005 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hermansky-Pudlak Syndrome 1 (HPS1, Accession NM_000195) is another VGAM172 host target gene. HPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPS1 BINDING SITE, designated SEQ ID:5696, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11559] Another function of VGAM172 is therefore inhibition of Hermansky-Pudlak Syndrome 1 (HPS1, Accession

NM_000195). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPS1. Mannosidase, Alpha, Class 1A, Member 1 (MAN1A1, Accession XM_166312) is another VGAM172 host target gene. MAN1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1A1 BINDING SITE, designated SEQ ID:44135, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11560] Another function of VGAM172 is therefore inhibition of Mannosidase, Alpha, Class 1A, Member 1 (MAN1A1, Accession XM_166312), a gene which removes 3 distinct mannose residues from peptide-bound Man(9)-GlcNAc(2) oligosaccharides. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1A1. The function of MAN1A1 has been established by previous studies. Man(9)-mannosidase (alpha-1,2-mannosidase 1A) catalyzes the removal of 3 distinct mannose residues from

peptide-bound Man(9)–GlcNAc(2) oligosaccharides. See MAN2A1 (OMIM Ref. No. 154582) for general information. Using an oligonucleotide probe derived from a pig liver Man(9)–mannosidase–specific cDNA template, Bause et al. (1993) isolated Man(9)–mannosidase from a human kidney cDNA library. The full-length cDNA predicted a 625–amino acid protein with a calculated molecular mass of 71 kD. Man(9)–mannosidase is a type II transmembrane protein with a short cytoplasmic polypeptide tail, a single transmembrane domain acting as a noncleavable signal sequence, a large luminal catalytic domain, and 3 potential N–glycosylation sites

[11561] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11562] Bause, E.; Bieberich, E.; Rolfs, A.; Volker, C.; Schmidt, B. : Molecular cloning and primary structure of Man(9)–mannosidase from human kidney. *Eur. J. Biochem.* 217: 535–540, 1993. ; and

[11563] Tremblay, L. O; Campbell Dyke, N.; Herscovics, A. : Molecular cloning, chromosomal mapping and tissue–specific expression of a novel human alpha–1,2–mannosidase gene involved in N–glycan.

[11564] Further studies establishing the function and utilities of MAN1A1 are found in John Hopkins OMIM database record ID 604344, and in cited publications numbered 4991–4992 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_007318) is another VGAM172 host target gene. PSEN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PSEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSEN1 BINDING SITE, designated SEQ ID:14236, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11565] Another function of VGAM172 is therefore inhibition of Presenilin 1 (Alzheimer disease 3) (PSEN1, Accession NM_007318). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSEN1. Solute Carrier Family 25 (mitochondrial carrier; ornithine transporter) Member 15 (SLC25A15, Accession NM_014252) is another VGAM172 host target gene. SLC25A15 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC25A15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC25A15 BINDING SITE, designated SEQ ID:15527, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11566] Another function of VGAM172 is therefore inhibition of Solute Carrier Family 25 (mitochondrial carrier; ornithine transporter) Member 15 (SLC25A15, Accession NM_014252), a gene which participates the ornithine transport across inner mitochondrial membrane, from the cytoplasm to the matrix. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC25A15. The function of SLC25A15 has been established by previous studies. The urea cycle is an example of metabolic homeostasis, maintaining concentrations of a toxic metabolite, ammonium ions, in a narrow, tolerable range despite more than 10-fold variations in dietary intake of its precursor, nitrogen. Five enzymes in 2 subcellular compartments (mitochondrial matrix and cytosol) ac-

comply with this feat. Another vital component of the urea cycle is the transporter required to move ornithine across the inner mitochondrial membrane from cytosol to mitochondrial matrix. This is the transporter that is defective in hyperornithinemia–hyperammonemia–homocitrullinuria (HHH syndrome; 238970). *Neurospora crassa* ARG13 and *Saccharomyces cerevisiae* ARG11 encode mitochondrial carrier family proteins that transport ornithine across the mitochondrial inner membrane. Camacho et al. (1999) used their sequences to identify EST candidates derived from genes that encode orthologous mammalian transporters. They thereby identified a gene, ORNT1, that maps to 13q14 and whose expression, similar to that of other urea cycle components, was high in liver and varied with changes in dietary protein. ORNT1 expression restored ornithine metabolism in fibroblasts from patients with HHH syndrome. They found that the ORNT1 gene encodes a 301-residue protein with 95% identity to mouse Ornt1 and 28% identity to *Neurospora* ARG13. Expression of either murine or human ORNT1 restored normal ornithine metabolism in HHH fibroblasts. The protein localized to mitochondria. In a survey of 11 HHH probands, Camacho et al. (1999) identified 3 ORNT1 mutant alleles that ac-

counted for 21 of 22 possible mutant ORNT1 genes in these patients

[11567] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11568] Camacho, J. A.; Obie, C.; Biery, B.; Goodman, B. K.; Hu, C.-A.; Almashanu, S.; Steel, G.; Casey, R.; Lambert, M.; Mitchell, G. A.; Valle, D. : Hyperornithinaemia-hyperammonaemia-homocitrullinuria syndrome is caused by mutations in a gene encoding a mitochondrial ornithine transporter. Nature Genet. 22: 151–158, 1999. ; and

[11569] Tsujino, S.; Kanazawa, N.; Ohashi, T.; Eto, Y.; Saito, T.; Kira, J.; Yamada, T. : Three novel mutations (G27E, in-sAAC, R179X) in the ORNT1 gene of Japanese patients with hyperornithinemia.

[11570] Further studies establishing the function and utilities of SLC25A15 are found in John Hopkins OMIM database record ID 603861, and in cited publications numbered 9450–7424 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM_130845) is another VGAM172 host target gene.

SNTB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNTB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNTB2 BINDING SITE, designated SEQ ID:28380, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11571] Another function of VGAM172 is therefore inhibition of Syntrophin, Beta 2 (dystrophin-associated protein A1, 59kDa, basic component 2) (SNTB2, Accession NM_130845). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNTB2. T-cell Acute Lymphocytic Leukemia 1 (TAL1, Accession NM_003189) is another VGAM172 host target gene. TAL1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAL1 BINDING SITE, designated SEQ ID:9176, to the nucleotide se-

quence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11572] Another function of VGAM172 is therefore inhibition of T-cell Acute Lymphocytic Leukemia 1 (TAL1, Accession NM_003189), a gene which may help control cell growth and differentiation. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAL1. The function of TAL1 has been established by previous studies. Finger et al. (1989) analyzed a t(1;14)(p32;q11) chromosomal translocation in a lymphohemopoietic stem cell line derived from a patient with acute T-lymphoblastic leukemia (Kurtzberg et al., 1985). The chromosomal joining of 14 to 1p occurred at the T-cell receptor delta diversity (D-delta-2) segment, and the reciprocal joining on chromosome 14 occurred at the T-cell delta diversity segment D-delta-1. Involvement of delta diversity segments at the translocation junctions suggested that the translocation occurred during an attempt at delta-1/delta-2 joining in a stem cell. Finger et al. (1989) found that the segment of chromosome 1 at band p32, adjacent to the chromosomal breakpoint, encodes a transcriptional unit designated TCL5. Finger et al. (1989) also demonstrated a rearrange-

ment of the TCL5 locus in a human melanoma cell line carrying a deletion at 1p32. The occurrence of 'biphenotypic' leukemias with lymphoid and myeloid characteristics and evidence of stem cell origin of myeloid, erythroid, megakaryocytic, and lymphoid lineages in chronic myeloid leukemia suggested that leukemias may arise from pluripotent hematopoietic cells. Begley et al. (1989) studied a leukemic stem cell line that was capable of differentiating into either myeloid or lymphoid cells and that carried a translocation between chromosomes 1 and 14, t(1;14)(p33;q11). By means of molecular cloning and sequencing, they showed that as a consequence of the translocation an unusual fusion transcript was generated. The chromosome 1 region involved in the breakpoint was the site of transcriptional activity apparently occurring only in hematopoietic tissues. Begley et al. (1989) concluded that the translocation may identify a gene located on chromosome 1 which is important for hematopoietic development and oncogenesis. They suggested the designation SCL (stem cell leukemia hematopoietic transcription factor).

[11573] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [11574] Begley, C. G.; Aplan, P. D.; Davey, M. P.; Nakahara, K.; Tchorz, K.; Kurtzberg, J.; Hershfield, M. S.; Haynes, B. F.; Cohen, D. I.; Waldmann, T. A.; Kirsch, I. R. : Chromosomal translocation in a human leukemic stem-cell line disrupts the T-cell antigen receptor delta-chain diversity region and results in a previously unreported fusion transcript. Proc. Nat. Acad. Sci. 86: 2031-2035, 1989. ; and
- [11575] Finger, L. R.; Kagan, J.; Christopher, G.; Kurtzberg, J.; Hershfield, M. S.; Nowell, P. C.; Croce, C. M. : Involvement of the TCL5 gene on human chromosome 1 in T-cell leukemia and mel.
- [11576] Further studies establishing the function and utilities of TAL1 are found in John Hopkins OMIM database record ID 187040, and in cited publications numbered 12610, 1261 and 2510-2521 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor-like 4 (TCFL4, Accession XM_032817) is another VGAM172 host target gene. TCFL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of TCFL4 BINDING SITE, designated SEQ ID:31772, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11577] Another function of VGAM172 is therefore inhibition of Transcription Factor-like 4 (TCFL4, Accession XM_032817), a gene which interacts with Mad and represses transcription by recruiting the Sin3A-histone deacetylase corepressor complex. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL4. The function of TCFL4 has been established by previous studies. Members of the basic helix-loop-helix leucine zipper (bHLH-Zip) family are transcription factors with roles in proliferation, determination, and differentiation (e.g., MAX; 154950). By searching sequence databases with a mouse Tcfl4 cDNA, Bjerknes and Cheng (1996) identified several TCFL4 expressed sequence tags derived from a variety of human tissues, and a 46-kb cosmid clone (GenBank U34879) containing the human TCFL4 gene. This cosmid, which maps to 17q21.1, also contains the HSD17B1 gene (OMIM Ref. No. 109684). The TCFL4 gene has 8 exons and spans more than 5 kb. The pre-

dicted TCFL4 protein contains a basic helix–loop–helix domain and a leucine zipper domain. RT–PCR detected mouse Tcfl4 expression in all tissues examined. In a 2–hybrid screen to identify Mad1 (OMIM Ref. No. 602686)–interacting proteins, Billin et al. (1999) identified TCFL4 as MLX, a bHLH–Zip protein that is structurally and functionally related to MAX. The predicted amino acid sequence of MLX is conserved at all positions that define the bHLH–Zip class of transcription factors and is most similar to that of MAX, sharing approximately 50% identity in the bHLH–Zip domains. The 244–amino acid human and mouse MLX proteins differ at only 4 amino acid positions. Billin et al. (1999) showed that transcriptional repression by Mad1:MLX heterodimers is dependent on dimerization, DNA binding, and recruitment of the Sin3A–histone deacetylase (see OMIM Ref. No. 601241) corepressor complex. Their findings suggested that MLX may act to diversify Mad family function by its restricted association with a subset of the Mad family of transcriptional repressors.

[11578] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11579] Billin, A. N.; Eilers, A. L.; Queva, C.; Ayer, D. E. : Mlx, a novel Max-like BHLHZip protein that interacts with the Max network of transcription factors. *J. Biol. Chem.* 274: 36344–36350, 1999. ; and
- [11580] Bjerknes, M.; Cheng, H. : TCFL4: a gene at 17q21.1 encoding a putative basic helix–loop–helix leucine–zipper transcription factor. *Gene* 181: 7–11, 1996.
- [11581] Further studies establishing the function and utilities of TCFL4 are found in John Hopkins OMIM database record ID 602976, and in cited publications numbered 8541–8543 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM172 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15356, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.
- [11582] Another function of VGAM172 is therefore inhibition of

Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 has been established by previous studies. Trichorhinophalangeal syndrome type I (OMIM Ref. No. 190350) is a malformation syndrome characterized by distinctive craniofacial and skeletal abnormalities and is inherited as an autosomal dominant. TRPS I patients have sparse scalp hair, bulbous tip of the nose, long flat philtrum, thin upper vermilion border, and protruding ears. Skeletal abnormalities include cone-shaped epiphyses at the phalanges, hip malformations, and short stature. Ludecke et al. (1995) and Hou et al. (1995) assigned the TRPS1 gene to 8q24. It maps centromeric to the gene that is mutant in multiple exostoses type I (EXT1; 133700); EXT1 is deleted in all patients with TRPS type II, or Langer-Giedion syndrome (OMIM Ref. No. 150230), which combines features of TRPS I and multiple exostoses. Momeni et al. (2000) positionally cloned a gene that spanned the chromosomal breakpoint in 2 patients with TRPS I and was deleted in 5 patients with TRPS I associ-

ated with an interstitial deletion. Northern blot analyses revealed transcripts of 7 and 10.5 kb. The gene, designated TRPS1, has 7 exons and encodes a polypeptide of 1,281 amino acids. The predicted protein sequence has 2 potential nuclear localization signals and an unusual combination of different zinc finger motifs, including IKAROS-like (see OMIM Ref. No. 603023) and GATA-binding (see OMIM Ref. No. 600576) sequences. Momeni et al. (2000) identified 6 different nonsense mutations in 10 unrelated patients. The findings suggested that haploinsufficiency for this putative transcription factor causes TRPS I. To investigate whether trichorhinophalangeal syndrome type III (OMIM Ref. No. 190351) is caused by TRPS1 mutations and to establish a genotype-phenotype correlation in TRPS, Ludecke et al. (2001) performed extensive mutation analysis and evaluated height and degree of brachydactyly in patients with TRPS I or TRPS III. They found 35 different mutations in 44 of 51 unrelated patients. The detection rate (86%) indicated that TRPS1 is the major locus for TRPS I and TRPS III. They found no mutation in the parents of sporadic patients or in apparently healthy relatives of familial patients, indicating complete penetrance of TRPS1 mutations. Evaluation of skeletal abnormalities of patients

with TRPS1 mutations revealed a wide clinical spectrum. The phenotype was variable in unrelated, age- and sex-matched patients with identical mutations, as well as in families. Four of the 5 missense mutations altered the GATA DNA-binding zinc finger, and 6 of the 7 unrelated patients with these mutations could be classified as having TRPS III, because they had severe bradycardia, due to short metacarpals, and severe short stature. The data indicated that TRPS III is at the severe end of the TRPS spectrum and that it is most often caused by a specific class of mutations in exon 6 the TRPS1 gene. In the study of Ludecke et al. (2001), 5 mutations were recurrent, and 4 of these were identified in patients of different ethnicities: 1 in patients of Norwegian, Turkish, and Belgian extraction, and another in patients of Belgian, Turkish, and Japanese extraction, for example.

[11583] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11584] Momeni, P.; Glockner, G.; Schmidt, O.; von Holtum, D.; Albrecht, B.; Gillessen-Kaesbach, G.; Hennekam, R.; Meinecke, P.; Zabel, B.; Rosenthal, A.; Horsthemke, B.; Ludecke, H.-J. : Mutations in a new gene, encoding a zinc-

finger protein, cause tricho-rhino-phalangeal syndrome type I. Nature Genet. 24: 71-74, 2000. ; and

[11585] Ludecke, H.-J.; Schaper, J.; Meinecke, P.; Momeni, P.; Gross, S.; von Holtum, D.; Hirche, H.; Abramowicz, M. J.; Albrecht, B.; Apacik, C.; Christen, H.-J.; Claussen, U.; and 28 others : G.

[11586] Further studies establishing the function and utilities of TRPS1 are found in John Hopkins OMIM database record ID 604386, and in cited publications numbered 7077-7078, 3619, 7945, 1268 and 12627 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 202 (ZNF202, Accession NM_003455) is another VGAM172 host target gene. ZNF202 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF202, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF202 BINDING SITE, designated SEQ ID:9512, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11587] Another function of VGAM172 is therefore inhibition of

Zinc Finger Protein 202 (ZNF202, Accession NM_003455). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF202. ARAP3 (Accession NM_022481) is another VGAM172 host target gene. ARAP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARAP3 BINDING SITE, designated SEQ ID:22856, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11588] Another function of VGAM172 is therefore inhibition of ARAP3 (Accession NM_022481). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARAP3. Bromodomain Containing 4 (BRD4, Accession NM_014299) is another VGAM172 host target gene. BRD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of BRD4 BINDING SITE, designated SEQ ID:15596, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11589] Another function of VGAM172 is therefore inhibition of Bromodomain Containing 4 (BRD4, Accession NM_014299). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRD4. Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175) is another VGAM172 host target gene. C8orf2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C8orf2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf2 BINDING SITE, designated SEQ ID:14026, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11590] Another function of VGAM172 is therefore inhibition of Chromosome 8 Open Reading Frame 2 (C8orf2, Accession NM_007175). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with C8orf2. FBP17 (Accession XM_052666) is another VGAM172 host target gene. FBP17 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FBP17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBP17 BINDING SITE, designated SEQ ID:36051, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11591] Another function of VGAM172 is therefore inhibition of FBP17 (Accession XM_052666). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBP17. FLJ00007 (Accession XM_048928) is another VGAM172 host target gene. FLJ00007 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ00007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00007 BINDING SITE, designated SEQ ID:35316, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2883.

[11592] Another function of VGAM172 is therefore inhibition of FLJ00007 (Accession XM_048928). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00007. FLJ14957 (Accession NM_032866) is another VGAM172 host target gene. FLJ14957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14957 BINDING SITE, designated SEQ ID:26686, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11593] Another function of VGAM172 is therefore inhibition of FLJ14957 (Accession NM_032866). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14957. FLJ31101 (Accession NM_017964) is another VGAM172 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31101, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19689, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11594] Another function of VGAM172 is therefore inhibition of FLJ31101 (Accession NM_017964). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31101. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044) is another VGAM172 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:17406 and SEQ ID:28928 respectively, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11595] Another function of VGAM172 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_015044). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. GTP Binding Protein 1 (GTPBP1, Accession NM_004286) is another VGAM172 host target gene. GTPBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTPBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTPBP1 BINDING SITE, designated SEQ ID:10499, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11596] Another function of VGAM172 is therefore inhibition of GTP Binding Protein 1 (GTPBP1, Accession NM_004286). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTPBP1. KIAA0711 (Accession NM_014867) is another VGAM172 host target gene. KIAA0711 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by KIAA0711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0711 BINDING SITE, designated SEQ ID:16959, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11597] Another function of VGAM172 is therefore inhibition of KIAA0711 (Accession NM_014867). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0711. KIAA0775 (Accession NM_014726) is another VGAM172 host target gene. KIAA0775 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0775, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0775 BINDING SITE, designated SEQ ID:16323, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11598] Another function of VGAM172 is therefore inhibition of

KIAA0775 (Accession NM_014726). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0775. KIAA1538 (Accession XM_049474) is another VGAM172 host target gene. KIAA1538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1538 BINDING SITE, designated SEQ ID:35438, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11599] Another function of VGAM172 is therefore inhibition of KIAA1538 (Accession XM_049474). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1538. KIAA1559 (Accession XM_054472) is another VGAM172 host target gene. KIAA1559 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1559, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA1559 BINDING SITE, designated SEQ ID:36167, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11600] Another function of VGAM172 is therefore inhibition of KIAA1559 (Accession XM_054472). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1559. KIAA1822 (Accession XM_041566) is another VGAM172 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33557, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11601] Another function of VGAM172 is therefore inhibition of KIAA1822 (Accession XM_041566). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. MGC21688 (Accession NM_144635) is another

VGAM172 host target gene. MGC21688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC21688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC21688 BINDING SITE, designated SEQ ID:29455, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11602] Another function of VGAM172 is therefore inhibition of MGC21688 (Accession NM_144635). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC21688. MGC3101 (Accession NM_024043) is another VGAM172 host target gene. MGC3101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3101 BINDING SITE, designated SEQ ID:23476, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11603] Another function of VGAM172 is therefore inhibition of MGC3101 (Accession NM_024043). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3101. Retinoic Acid Induced 16 (RAI16, Accession NM_022749) is another VGAM172 host target gene. RAI16 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RAI16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI16 BINDING SITE, designated SEQ ID:22972, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11604] Another function of VGAM172 is therefore inhibition of Retinoic Acid Induced 16 (RAI16, Accession NM_022749). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI16. RDC1 (Accession XM_051522) is another VGAM172 host target gene. RDC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RDC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDC1 BINDING SITE, designated SEQ ID:35849, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11605] Another function of VGAM172 is therefore inhibition of RDC1 (Accession XM_051522). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDC1. RING1 and YY1 Binding Protein (RYBP, Accession XM_002853) is another VGAM172 host target gene. RYBP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RYBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RYBP BINDING SITE, designated SEQ ID:29909, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11606] Another function of VGAM172 is therefore inhibition of RING1 and YY1 Binding Protein (RYBP, Accession XM_002853). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with RYBP. Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263) is another VGAM172 host target gene. SEMA4F BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SEMA4F, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA4F BINDING SITE, designated SEQ ID:10462, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11607] Another function of VGAM172 is therefore inhibition of Sema Domain, Immunoglobulin Domain (Ig), Transmembrane Domain (TM) and Short Cytoplasmic Domain, (semaphorin) 4F (SEMA4F, Accession NM_004263). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA4F. SPEC1 (Accession NM_020239) is another VGAM172 host target gene. SPEC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SPEC1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPEC1 BINDING SITE, designated SEQ ID:21513, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11608] Another function of VGAM172 is therefore inhibition of SPEC1 (Accession NM_020239). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPEC1. Tripartite Motif-containing 5 (TRIM5, Accession NM_033093) is another VGAM172 host target gene. TRIM5 BINDING SITE1 through TRIM5 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TRIM5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM5 BINDING SITE1 through TRIM5 BINDING SITE3, designated SEQ ID:26937, SEQ ID:26927 and SEQ ID:26936 respectively, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11609] Another function of VGAM172 is therefore inhibition of

Tripartite Motif-containing 5 (TRIM5, Accession NM_033093). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM5. LOC115110 (Accession XM_049825) is another VGAM172 host target gene. LOC115110 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115110 BINDING SITE, designated SEQ ID:35511, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11610] Another function of VGAM172 is therefore inhibition of LOC115110 (Accession XM_049825). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115110. LOC127428 (Accession XM_059144) is another VGAM172 host target gene. LOC127428 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC127428, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127428 BINDING SITE, designated SEQ ID:36901, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11611] Another function of VGAM172 is therefore inhibition of LOC127428 (Accession XM_059144). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127428. LOC145662 (Accession XM_085194) is another VGAM172 host target gene. LOC145662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145662 BINDING SITE, designated SEQ ID:37919, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11612] Another function of VGAM172 is therefore inhibition of LOC145662 (Accession XM_085194). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145662. LOC146443 (Accession XM_085461) is another VGAM172 host target gene. LOC146443 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146443 BINDING SITE, designated SEQ ID:38150, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11613] Another function of VGAM172 is therefore inhibition of LOC146443 (Accession XM_085461). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146443. LOC149372 (Accession XM_086509) is another VGAM172 host target gene. LOC149372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149372 BINDING SITE, designated SEQ ID:38731, to the nucleotide sequence of VGAM172 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2883.

[11614] Another function of VGAM172 is therefore inhibition of LOC149372 (Accession XM_086509). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149372. LOC151438 (Accession XM_098060) is another VGAM172 host target gene. LOC151438 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151438, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151438 BINDING SITE, designated SEQ ID:41348, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11615] Another function of VGAM172 is therefore inhibition of LOC151438 (Accession XM_098060). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151438. LOC151657 (Accession XM_098100) is another VGAM172 host target gene. LOC151657 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151657, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151657 BINDING SITE, designated SEQ ID:41383, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11616] Another function of VGAM172 is therefore inhibition of LOC151657 (Accession XM_098100). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151657. LOC151877 (Accession XM_098132) is another VGAM172 host target gene. LOC151877 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151877, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151877 BINDING SITE, designated SEQ ID:41399, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11617] Another function of VGAM172 is therefore inhibition of LOC151877 (Accession XM_098132). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC151877. LOC157931 (Accession XM_098845) is another VGAM172 host target gene. LOC157931 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157931 BINDING SITE, designated SEQ ID:41906, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11618] Another function of VGAM172 is therefore inhibition of LOC157931 (Accession XM_098845). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157931. LOC205251 (Accession XM_119554) is another VGAM172 host target gene. LOC205251 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205251 BINDING SITE, designated SEQ ID:43589, to

the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11619] Another function of VGAM172 is therefore inhibition of LOC205251 (Accession XM_119554). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205251. LOC255177 (Accession XM_172941) is another VGAM172 host target gene. LOC255177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255177 BINDING SITE, designated SEQ ID:46205, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11620] Another function of VGAM172 is therefore inhibition of LOC255177 (Accession XM_172941). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255177. LOC256021 (Accession XM_172884) is another VGAM172 host target gene. LOC256021 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC256021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256021 BINDING SITE, designated SEQ ID:46168, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11621] Another function of VGAM172 is therefore inhibition of LOC256021 (Accession XM_172884). Accordingly, utilities of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256021. LOC51301 (Accession NM_016591) is another VGAM172 host target gene. LOC51301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51301 BINDING SITE, designated SEQ ID:18675, to the nucleotide sequence of VGAM172 RNA, herein designated VGAM RNA, also designated SEQ ID:2883.

[11622] Another function of VGAM172 is therefore inhibition of LOC51301 (Accession NM_016591). Accordingly, utilities

of VGAM172 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51301. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 173 (VGAM173) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11623] VGAM173 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM173 was detected is described hereinabove with reference to Figs. 1–8.

[11624] VGAM173 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11625] VGAM173 gene encodes a VGAM173 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM173 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM173 precursor RNA is designated SEQ ID:159, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:159 is located at position 272848 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11626] VGAM173 precursor RNA folds onto itself, forming VGAM173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11627] An enzyme complex designated DICER COMPLEX, `dices` the VGAM173 folded precursor RNA into VGAM173 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide se-

quence of VGAM173 RNA is designated SEQ ID:2884, and is provided hereinbelow with reference to the sequence listing part.

[11628] VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM173 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11629] VGAM173 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM173 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM173 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[11630] The complementary binding of VGAM173 RNA, herein designated VGAM RNA, to host target binding sites on VGAM173 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM173 host target RNA into VGAM173 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11631] It is appreciated that VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM173 host target genes. The mRNA of each one of this plurality of VGAM173 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM173 RNA, herein designated VGAM RNA, and which when bound by VGAM173 RNA causes inhibition of translation of respective one or more VGAM173 host target proteins.

[11632] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM173 gene, herein designated VGAM GENE, on one or more VGAM173 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11633] It is yet further appreciated that a function of VGAM173 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM173 correlate with, and may be deduced from, the identity of the host target genes which VGAM173 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11634] Nucleotide sequences of the VGAM173 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM173 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM173 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM173 are further described hereinbelow with reference to Table 1.

[11635] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM173 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM173 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[11636] As mentioned hereinabove with reference to Fig. 1, a function of VGAM173 gene, herein designated VGAM is inhibition of expression of VGAM173 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM173 correlate with, and may be deduced from, the identity of the target genes which VGAM173 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11637] Beta-site APP-cleaving Enzyme (BACE, Accession NM_012104) is a VGAM173 host target gene. BACE BINDING SITE1 and BACE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BACE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACE BINDING SITE1 and BACE BINDING SITE2, designated SEQ ID:14418 and SEQ ID:29086 respectively, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11638] A function of VGAM173 is therefore inhibition of Beta-site APP-cleaving Enzyme (BACE, Accession NM_012104), a

gene which is responsible for the proteolytic processing of the amyloid precursor protein. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACE. The function of BACE has been established by previous studies. Cerebral deposition of amyloid beta peptide is an early and critical feature of Alzheimer disease (AD; 104300). Amyloid beta generation depends on proteolytic cleavage of amyloid precursor protein (APP; 104760) by 2 proteases, beta-secretase and gamma-secretase. Vassar et al. (1999) reported the cloning of a human transmembrane aspartic protease that had all the known characteristics of the beta-secretase. Using an expression cloning strategy, they identified a clone that shared significant sequence similarity with members of the pepsin subfamily of aspartic proteases. This clone encoded a novel protein, designated BACE for 'beta-site APP-cleaving enzyme.' The BACE open reading frame encodes a protein of 501 amino acids containing a 21-amino acid signal peptide followed by a proprotein domain spanning amino acids 22 to 45. The luminal domain of the mature protein is followed by 1 predicted transmembrane domain and a short cytosolic C-terminal tail of 24 amino acids. BACE was predicted to

be a type 1 transmembrane protein with the active site on the luminal side of the membrane, where beta-secretase cleaves APP. The BACE protein shares greatest amino acid identity (30%) with cathepsin E (OMIM Ref. No. 116890). Rat and mouse BACE orthologs have 96% amino acid sequence identity with the human BACE protein. Northern blot analysis of human BACE mRNA in adult peripheral tissues and various subregions of the brain detected 3 transcripts of approximately 7.0, 4.4, and 2.6 kb. By in situ hybridization, expression of BACE mRNA in rat brain was observed at higher levels in neurons than in glia, supporting the idea that neurons are the primary source of the extracellular A-beta deposited in amyloid plaques. Vassar et al. (1999) ascribed the difference between the apparent and calculated molecular weight (approximately 70 and 51 kD, respectively) of the BACE protein to N-linked glycosylation. Immunostaining demonstrated intracellular localization of BACE to the Golgi and endosomes. Transient overexpression of BACE did not affect APP expression, but decreased alpha-secretase cleavage and increased beta-secretase activity in cells expressing wildtype or Swedish mutant (104760.0008) APP. BACE overexpression induced cleavage only at the known beta-secretase positions, asp1

and glu11. Vassar et al. (1999) concluded that their data provided strong evidence that the BACE aspartic protease is the long-sought beta-secretase. Animal model experiments lend further support to the function of BACE. Luo et al. (2001) found that mice deficient in BACE1 are healthy, fertile, and appear normal in gross anatomy, tissue histology, hematology, and clinical chemistry. Bace1 -/- mice who are also hemizygous for an amyloid precursor protein transgene lack brain beta-amyloid and beta-secretase-cleaved APP C-terminal fragments. These results provided validation of BACE1 as the major beta-secretase in vivo and suggested that therapeutic inhibition of BACE1 for the treatment of Alzheimer disease may be free of mechanism-based toxicity.

[11639] It is appreciated that the abovementioned animal model for BACE is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11640] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11641] Vassar, R.; Bennett, B. D.; Babu-Khan, S.; Kahn, S.; Mendiaz, E. A.; Dents, P.; Taplow, D. B.; Ross, S.; Amaranta, P.;

Loeloff, R.; Luo, Y.; Fisher, S.; and 12 others : Beta-secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE. Science 286: 735–741, 1999. ; and

[11642] Luo, Y.; Bolon, B.; Kahn, S.; Bennett, B. D.; Babu-Khan, S.; Denis, P.; Fan, W.; Kha, H.; Zhang, J.; Gong, Y.; Martin, L.; Louis, J.-C.; Yan, Q.; Richards, W. G.; Citron, M.; Vassar, R.

[11643] Further studies establishing the function and utilities of BACE are found in John Hopkins OMIM database record ID 604252, and in cited publications numbered 5405, 5418–5422, 12307–7054, 7067, 7064–706 and 7068 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LIM Domain Kinase 1 (LIMK1, Accession NM_002314) is another VGAM173 host target gene. LIMK1 BINDING SITE1 and LIMK1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LIMK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE1 and LIMK1 BINDING SITE2, designated SEQ ID:8124 and SEQ ID:18799 respectively, to the nucleotide sequence of VGAM173 RNA, herein designated

VGAM RNA, also designated SEQ ID:2884.

[11644] Another function of VGAM173 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_002314). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037) is another VGAM173 host target gene. LRP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LRP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP4 BINDING SITE, designated SEQ ID:32198, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11645] Another function of VGAM173 is therefore inhibition of Low Density Lipoprotein Receptor-related Protein 4 (LRP4, Accession XM_035037). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP4. Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession

NM_002608) is another VGAM173 host target gene.

PDGFB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PDGFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFB BINDING SITE, designated SEQ ID:8469, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11646] Another function of VGAM173 is therefore inhibition of Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession NM_002608), a gene which plays an important role in stimulating adjacent cells to grow and thereby heal the wound. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFB. The function of PDGFB has been established by previous studies. Most proliferating cells are programmed to undergo apoptosis unless specific survival signals are provided. Platelet-derived growth factor promotes cellular proliferation and inhibits apoptosis. Romashkova and Makarov (1999) showed that PDGF activates the RAS/PIK3/AKT1/IKK/NFKB1 pathway. In this

pathway, NFKB1 (OMIM Ref. No. 164011) does not induce c-myc and apoptosis, but instead induces putative anti-apoptotic genes. In response to PDGF, AKT1 (OMIM Ref. No. 164730) transiently associates with IKK (see OMIM Ref. No. 600664) and induces IKK activation. The authors suggested that under certain conditions PIK3 (see OMIM Ref. No. 171834) may activate NFKB1 without the involvement of NFKBIA (OMIM Ref. No. 164008) or NFKBIB (OMIM Ref. No. 604495) degradation. Dermatofibrosarcoma protuberans (DFSP), an infiltrative skin tumor of intermediate malignancy, presents specific cytogenetic features such as reciprocal translocations t(17;22)(q22;q13) and supernumerary ring chromosomes derived from t(17;22). Simon et al. (1997) characterized the breakpoints from translocations and rings in dermatofibrosarcoma protuberans and its juvenile form, giant cell fibroblastoma, on the genomic and RNA levels. They found that these rearrangements fuse the PDGFB gene and the COL1A1 gene (OMIM Ref. No. 120150). Simon et al. (1997) commented that PDGFB has transforming activity and is a potent mitogen for a number of cell types, but its role in oncogenic processes was not fully understood. They noted that neither COL1A1 nor PDGFB had hitherto been implicated in tumor translo-

cations. The gene fusions deleted exon 1 of PDGFB and released this growth factor from its normal regulation; see 190040.0002.

[11647] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11648] Simon, M.-P.; Pedeutour, F.; Sirvent, N.; Grosgeorge, J.; Minoletti, F.; Coindre, J.-M.; Terrier-Lacombe, M.-J.; Mandahl, N.; Craver, R. D.; Blin, N.; Sozzi, G.; Turc-Carel, C.; O'Brien, K. P.; Kedra, D.; Fransson, I.; Guilbaud, C.; Dumanski, J. P. : Deregulation of the platelet-derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma. *Nature Genet.* 15: 95-98, 1997. ; and

[11649] Josephs, S. F.; Guo, C.; Ratner, L.; Wong-Staal, F. : Human proto-oncogene nucleotide sequences corresponding to the transforming region of simian sarcoma virus. *Science* 223: 487-491, 1983.

[11650] Further studies establishing the function and utilities of PDGFB are found in John Hopkins OMIM database record ID 190040, and in cited publications numbered 10481-10491, 9741, 9745-9747, 10094-9750, 3292-3294, 9751-9753, 3533, 9754-9758, 12740,

9764, 11491, 976 and 10480 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Smcx Homolog, X Chromosome (mouse) (SMCX, Accession NM_004187) is another VGAM173 host target gene. SMCX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMCX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMCX BINDING SITE, designated SEQ ID:10395, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11651] Another function of VGAM173 is therefore inhibition of Smcx Homolog, X Chromosome (mouse) (SMCX, Accession NM_004187), a gene which escapes X inactivation. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMCX. The function of SMCX and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6,

Accession NM_017662) is another VGAM173 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19198, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11652] Another function of VGAM173 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of TRPM6 has been established by previous studies. Schlingmann et al. (2002) and Walder et al. (2002) studied hypomagnesemia with secondary hypocalcemia (HSH; 602014), which maps to 9q22, and by positional cloning identified the TRPM6 gene as the site of causative mutations. Walder et al. (2002) found that the complete cDNA sequence of

TRPM6 contains 8,429 nucleotides, including an open reading frame of 6,069 nucleotides. The predicted TRPM6 protein contains 2,022 amino acids, has a calculated molecular mass of roughly 234 kD, and contains a predicted ion channel domain and a protein kinase domain. Northern blot analysis detected an 8.5-kb transcript abundantly expressed in kidney and colon. By in situ hybridization to various human tissues, Schlingmann et al. (2002) observed TRPM6 mRNA in colon epithelial cells, duodenum, jejunum, and ileum. Schlingmann et al. (2002) studied 5 families (2 Turkish, 1 Swedish, 1 Israeli, and 1 Albanian) with typical HSH and discovered 7 mutations in the TRPM6 gene; the Swedish and Israeli families were nonconsanguineous and the affected children were compound heterozygotes for TRPM6 mutations. The age at onset of symptoms varied from 3 weeks to 4 months. Neurologic symptoms included tetany, muscle spasms, and seizures due to hypomagnesemic hypocalcemia. Walder et al. (2002) identified mutations in the TRPM6 gene in 7 families: 3 Bedouin Arab families from Israel, 1 Arab family from Greece, a family in Germany, and 2 additional Arab families from Israel. This was the first case of a human disorder attributed to mutation in a channel ki-

nase.

[11653] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11654] Walder, R. Y.; Landau, D.; Meyer, P.; Shalev, H.; Tsolia, M.; Borochowitz, Z.; Boettger, M. B.; Beck, G. E.; Englehardt, R. K.; Carmi, R.; Sheffield, V. C. : Mutation of TRPM6 causes familial hypomagnesemia with secondary hypocalcemia. Nature Genet. 31: 171–174, 2002. ; and

[11655] Schlingmann, K. P.; Weber, S.; Peters, M.; Nejsum, L. N.; Vitzthum, H.; Klingel, K.; Kratz, M.; Haddad, E.; Ristoff, E.; Dinour, D.; Syrrou, M.; Nielsen, S.; Sassen, M.; Waldegger, S.; S.

[11656] Further studies establishing the function and utilities of TRPM6 are found in John Hopkins OMIM database record ID 607009, and in cited publications numbered 592 and 6145 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 42 (myeloid–specific retinoic acid– responsive) (ZNF42, Accession NM_003422) is another VGAM173 host target gene. ZNF42 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF42, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF42 BINDING SITE, designated SEQ ID:9467, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11657] Another function of VGAM173 is therefore inhibition of Zinc Finger Protein 42 (myeloid-specific retinoic acid- responsive) (ZNF42, Accession NM_003422), a gene which may be one regulator of transcriptional events during hemopoietic development. Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF42. The function of ZNF42 has been established by previous studies. Zinc finger genes encode metal-binding proteins that can act as transcriptional regulators of other genes. In an effort to identify activators of the genetic cascade in hemopoietic differentiation, Hromas et al. (1991) used degenerate synthetic oligonucleotides to the conserved zinc finger histidine-cysteine link to probe a human myeloid lambda gt11 cDNA library. One of the cDNA clones obtained hybridized preferentially to mRNA from myeloid cells. Sequence analysis of the coding region for the gene

demonstrated 13 zinc finger regions and a glycine–proline–rich region between the fourth and fifth zinc finger domains. The gene was localized to 19q13.2–q13.4 by chromosomal in situ hybridization, confirmed by hybridization of a labeled probe to dot blots of flow–sorted chromosomes. Chromosome 19 contains other zinc finger genes, e.g., ZFP36 (OMIM Ref. No. 190700), which is located at 19q13.1. The new zinc finger gene, which they designated MZF–1 for 'myeloid zinc finger,' was preferentially expressed in myeloid leukemia cell lines, with the highest mRNA levels noted in cells induced to differentiate with retinoic acid. The ZNF42 gene may be a regulator of transcriptional events during hemopoietic development. The myeloid zinc finger gene 1 (MZF1) is a putative transcription factor of the C2H2 zinc finger gene family. Morris et al. (1995) found that MZF1 regulates the CD34 promoter (OMIM Ref. No. 142230) in a tissue–specific manner. They had previously demonstrated MZF–1 binding sites in the promoters of several genes expressed during myeloid differentiation.

[11658] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11659] Hromas, R.; Collins, S. J.; Hickstein, D.; Raskind, W.; Deaven, L. L.; O'Hara, P.; Hagen, F. S.; Kaushansky, K. : A retinoic acid-responsive human zinc finger gene, MZF-1, preferentially expressed in myeloid cells. J. Biol. Chem. 266: 14183-14187, 1991. ; and
- [11660] Morris, J. F.; Rauscher, F. J., III; Davis, B.; Klemsz, M.; Xu, D.; Tenen, D.; Hromas, R. : The myeloid zinc finger gene, MZF-1, regulates the CD34 promoter in vitro. Blood 86: 3640-3647.
- [11661] Further studies establishing the function and utilities of ZNF42 are found in John Hopkins OMIM database record ID 194550, and in cited publications numbered 522-523 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 74 (Cos52) (ZNF74, Accession NM_003426) is another VGAM173 host target gene. ZNF74 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF74, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF74 BINDING SITE, designated SEQ ID:9472, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2884.

[11662] Another function of VGAM173 is therefore inhibition of Zinc Finger Protein 74 (Cos52) (ZNF74, Accession NM_003426). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF74. COAS3 (Accession NM_139020) is another VGAM173 host target gene. COAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COAS3 BINDING SITE, designated SEQ ID:29122, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11663] Another function of VGAM173 is therefore inhibition of COAS3 (Accession NM_139020). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COAS3. FLJ10408 (Accession NM_018088) is another VGAM173 host target gene. FLJ10408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by FLJ10408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10408 BINDING SITE, designated SEQ ID:19850, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11664] Another function of VGAM173 is therefore inhibition of FLJ10408 (Accession NM_018088). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10408. FLJ12707 (Accession NM_022067) is another VGAM173 host target gene. FLJ12707 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12707 BINDING SITE, designated SEQ ID:22609, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11665] Another function of VGAM173 is therefore inhibition of FLJ12707 (Accession NM_022067). Accordingly, utilities of

VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12707. FLJ13204 (Accession NM_024761) is another VGAM173 host target gene. FLJ13204 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13204, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13204 BINDING SITE, designated SEQ ID:24115, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11666] Another function of VGAM173 is therefore inhibition of FLJ13204 (Accession NM_024761). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13204. Interleukin 18 Binding Protein (IL18BP, Accession NM_005699) is another VGAM173 host target gene. IL18BP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL18BP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of IL18BP BINDING SITE, designated SEQ ID:12251, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11667] Another function of VGAM173 is therefore inhibition of Interleukin 18 Binding Protein (IL18BP, Accession NM_005699). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL18BP. KIAA0089 (Accession XM_046056) is another VGAM173 host target gene. KIAA0089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0089 BINDING SITE, designated SEQ ID:34664, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11668] Another function of VGAM173 is therefore inhibition of KIAA0089 (Accession XM_046056). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0089. KIAA0410 (Accession NM_014778) is another VGAM173 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16618, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11669] Another function of VGAM173 is therefore inhibition of KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0410. KIAA0459 (Accession XM_027862) is another VGAM173 host target gene. KIAA0459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0459 BINDING SITE, designated SEQ ID:30573, to the nucleotide sequence of VGAM173 RNA, herein designated

VGAM RNA, also designated SEQ ID:2884.

[11670] Another function of VGAM173 is therefore inhibition of KIAA0459 (Accession XM_027862). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0459. KIAA0534 (Accession XM_049349) is another VGAM173 host target gene. KIAA0534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0534 BINDING SITE, designated SEQ ID:35383, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11671] Another function of VGAM173 is therefore inhibition of KIAA0534 (Accession XM_049349). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0534. KIAA1755 (Accession XM_028810) is another VGAM173 host target gene. KIAA1755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1755, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1755 BINDING SITE, designated SEQ ID:30749, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11672] Another function of VGAM173 is therefore inhibition of KIAA1755 (Accession XM_028810). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1755. MGC9753 (Accession NM_033419) is another VGAM173 host target gene. MGC9753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC9753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9753 BINDING SITE, designated SEQ ID:27241, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11673] Another function of VGAM173 is therefore inhibition of MGC9753 (Accession NM_033419). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with MGC9753. MPPE1 (Accession NM_023075) is another VGAM173 host target gene. MPPE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MPPE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPPE1 BINDING SITE, designated SEQ ID:23332, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11674] Another function of VGAM173 is therefore inhibition of MPPE1 (Accession NM_023075). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPPE1. Phospholipid Scramblase 3 (PLSCR3, Accession NM_020360) is another VGAM173 host target gene. PLSCR3 BINDING SITE1 and PLSCR3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PLSCR3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR3 BINDING

SITE1 and PLSCR3 BINDING SITE2, designated SEQ ID:21632 and SEQ ID:43637 respectively, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11675] Another function of VGAM173 is therefore inhibition of Phospholipid Scramblase 3 (PLSCR3, Accession NM_020360). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR3. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942) is another VGAM173 host target gene. RPS6KA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA4 BINDING SITE, designated SEQ ID:10054, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11676] Another function of VGAM173 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942). Accordingly, utilities of

VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA4. SET Binding Protein 1 (SETBP1, Accession NM_015559) is another VGAM173 host target gene. SETBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SETBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SETBP1 BINDING SITE, designated SEQ ID:17825, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11677] Another function of VGAM173 is therefore inhibition of SET Binding Protein 1 (SETBP1, Accession NM_015559). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SETBP1. LOC113523 (Accession XM_054378) is another VGAM173 host target gene. LOC113523 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113523, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC113523 BINDING SITE, designated SEQ ID:36157, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11678] Another function of VGAM173 is therefore inhibition of LOC113523 (Accession XM_054378). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113523. LOC124987 (Accession XM_064384) is another VGAM173 host target gene. LOC124987 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124987 BINDING SITE, designated SEQ ID:37265, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11679] Another function of VGAM173 is therefore inhibition of LOC124987 (Accession XM_064384). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124987. LOC127281 (Accession XM_059128) is an-

other VGAM173 host target gene. LOC127281 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127281, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127281 BINDING SITE, designated SEQ ID:36888, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11680] Another function of VGAM173 is therefore inhibition of LOC127281 (Accession XM_059128). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127281. LOC143425 (Accession XM_113695) is another VGAM173 host target gene. LOC143425 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143425, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143425 BINDING SITE, designated SEQ ID:42353, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11681] Another function of VGAM173 is therefore inhibition of LOC143425 (Accession XM_113695). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143425. LOC145195 (Accession XM_096731) is another VGAM173 host target gene. LOC145195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145195 BINDING SITE, designated SEQ ID:40514, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11682] Another function of VGAM173 is therefore inhibition of LOC145195 (Accession XM_096731). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145195. LOC145719 (Accession XM_096848) is another VGAM173 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40574, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11683] Another function of VGAM173 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM173 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40563, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11684] Another function of VGAM173 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145720. LOC148029 (Accession XM_086014) is another VGAM173 host target gene. LOC148029 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148029 BINDING SITE, designated SEQ ID:38444, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11685] Another function of VGAM173 is therefore inhibition of LOC148029 (Accession XM_086014). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148029. LOC150290 (Accession XM_086863) is another VGAM173 host target gene. LOC150290 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150290 BINDING SITE, designated SEQ ID:38932, to the nucleotide sequence of VGAM173 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2884.

[11686] Another function of VGAM173 is therefore inhibition of LOC150290 (Accession XM_086863). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150290. LOC152698 (Accession XM_017241) is another VGAM173 host target gene. LOC152698 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152698, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152698 BINDING SITE, designated SEQ ID:30312, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11687] Another function of VGAM173 is therefore inhibition of LOC152698 (Accession XM_017241). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152698. LOC153894 (Accession XM_087796) is another VGAM173 host target gene. LOC153894 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153894, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153894 BINDING SITE, designated SEQ ID:39427, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11688] Another function of VGAM173 is therefore inhibition of LOC153894 (Accession XM_087796). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153894. LOC157280 (Accession XM_058301) is another VGAM173 host target gene. LOC157280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157280 BINDING SITE, designated SEQ ID:36593, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11689] Another function of VGAM173 is therefore inhibition of LOC157280 (Accession XM_058301). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC157280. LOC158062 (Accession XM_098861) is another VGAM173 host target gene. LOC158062 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158062, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158062 BINDING SITE, designated SEQ ID:41914, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11690] Another function of VGAM173 is therefore inhibition of LOC158062 (Accession XM_098861). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158062. LOC197114 (Accession XM_116987) is another VGAM173 host target gene. LOC197114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197114 BINDING SITE, designated SEQ ID:43187, to

the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11691] Another function of VGAM173 is therefore inhibition of LOC197114 (Accession XM_116987). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197114. LOC200933 (Accession XM_117294) is another VGAM173 host target gene. LOC200933 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200933, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200933 BINDING SITE, designated SEQ ID:43365, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11692] Another function of VGAM173 is therefore inhibition of LOC200933 (Accession XM_117294). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200933. LOC255448 (Accession XM_170623) is another VGAM173 host target gene. LOC255448 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC255448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255448 BINDING SITE, designated SEQ ID:45403, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11693] Another function of VGAM173 is therefore inhibition of LOC255448 (Accession XM_170623). Accordingly, utilities of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255448. LOC91050 (Accession XM_035703) is another VGAM173 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32335, to the nucleotide sequence of VGAM173 RNA, herein designated VGAM RNA, also designated SEQ ID:2884.

[11694] Another function of VGAM173 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities

of VGAM173 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 174 (VGAM174) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11695] VGAM174 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM174 was detected is described hereinabove with reference to Figs. 1-8.

[11696] VGAM174 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11697] VGAM174 gene encodes a VGAM174 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM174 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se-

quence of VGAM174 precursor RNA is designated SEQ ID:160, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:160 is located at position 86647 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11698] VGAM174 precursor RNA folds onto itself, forming VGAM174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11699] An enzyme complex designated DICER COMPLEX, `dices` the VGAM174 folded precursor RNA into VGAM174 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide se-

quence of VGAM174 RNA is designated SEQ ID:2885, and is provided hereinbelow with reference to the sequence listing part.

[11700] VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM174 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11701] VGAM174 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM174 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM174 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[11702] The complementary binding of VGAM174 RNA, herein designated VGAM RNA, to host target binding sites on VGAM174 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM174 host target RNA into VGAM174 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11703] It is appreciated that VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM174 host target genes. The mRNA of each one of this plurality of VGAM174 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM174 RNA, herein designated VGAM RNA, and which when bound by VGAM174 RNA causes inhibition of translation of respective one or more VGAM174 host target proteins.

[11704] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM174 gene, herein designated VGAM GENE, on one or more VGAM174 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11705] It is yet further appreciated that a function of VGAM174 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM174 correlate with, and may be deduced from, the identity of the host target genes which VGAM174 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11706] Nucleotide sequences of the VGAM174 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM174 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM174 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM174 are further described hereinbelow with reference to Table 1.

[11707] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM174 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM174 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[11708] As mentioned hereinabove with reference to Fig. 1, a function of VGAM174 gene, herein designated VGAM is inhibition of expression of VGAM174 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM174 correlate with, and may be deduced from, the identity of the target genes which VGAM174 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11709] D8S2298E (Accession NM_005671) is a VGAM174 host target gene. D8S2298E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D8S2298E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D8S2298E BINDING SITE, designated SEQ ID:12229, to the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, also designated SEQ ID:2885.

[11710] A function of VGAM174 is therefore inhibition of D8S2298E (Accession NM_005671). Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

D8S2298E. Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM_168542) is another VGAM174 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated SEQ ID:45224, to the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, also designated SEQ ID:2885.

[11711] Another function of VGAM174 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF has been established by previous studies. Kilby et al. (1996) found that the protein and mRNA for both hepatocyte growth factor and its receptor (MET) are present in third trimester placentas, suggesting that HGF serves as a paracrine mediator to control placen-

tal development and growth. B cells develop in the bone marrow from progenitor cells that have been designated pre-pro-B cells, pro-B cells (no immunoglobulin, or Ig, chains chosen), pre-B cells (which have selected a heavy chain but not a light chain), and finally B cells (which express both heavy and light chains of the Ig molecule). Differentiation of pre-pro-B cells to pro-B cells requires signaling through IL7 receptor (IL7R; 146661) mediated by the pre-pro-B cell growth-stimulating factor (PPBSF), which consists of IL7 (OMIM Ref. No. 146660) and a 30-kD protein cofactor. By amino acid sequencing and RT-PCR analysis, Lai and Goldschneider (2001) determined that the PPBSF cofactor is the 30-kD beta chain of HGF (HGFB) produced independently of the 60-kD alpha chain of HGF. Formation of an IL7-HGFB heterodimer requires the presence of heparin sulfate. Functional analysis indicated that either IL7 or HGFB can maintain the viability of pre-pro-B cells, but only the heterodimer can stimulate their proliferation and differentiation into pro-B cells. Lai and Goldschneider (2001) concluded that PPBSF is a novel form of cytokine, a hybrid cytokine, consisting of the bioactive components of 2 unrelated cytokines. They proposed that through its heparin-binding and mitogenic

properties, HGFB enables IL7 to participate in cognate interactions at the stromal cell surface and transduce signals effectively at low levels of IL7R. Animal model experiments lend further support to the function of HGF.

Schmidt et al. (1995) and Uehara et al. (1995) produced targeted disruption of the HGF gene in mice and found that mice lacking the gene product fail to develop completely and die in utero. The mutation affects the embryonic liver, which is reduced in size and shows extensive loss of parenchymal cells. In addition, development of the placenta, particularly of trophoblast cells, is impaired.

HGF/SF is thought to mediate a signal exchange between the mesenchyme and epithelia during mouse development. Both the HGF gene and the gene for its receptor, the product of the MET protooncogene, are expressed in many tissues during embryonic development and in the adult. The findings of these studies indicate that HGF/SF is an essential mediator of allantoic mesenchyme-trophoblastic epithelia interaction required for placental organogenesis.

[11712] It is appreciated that the abovementioned animal model for HGF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre-

ciated from the publications sited hereinbelow.

[11713] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11714] Lai, L.; Goldschneider, I. : Cutting edge: identification of a hybrid cytokine consisting of IL-7 and the beta-chain of the hepatocyte growth factor/scatter factor. J. Immun. 167: 3550-3554, 2001. ; and

[11715] Schmidt, C.; Bladt, F.; Goedecke, S.; Brinkmann, V.; Zschiesche, W.; Sharpe, M.; Gherardi, E.; Birchmeier, C. : Scatter factor/hepatocyte growth factor is essential for liver development.

[11716] Further studies establishing the function and utilities of HGF are found in John Hopkins OMIM database record ID 142409, and in sited publications numbered 11303-11306, 2603, 11307-1131 and 12288-11319 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1755 (Accession XM_028810) is another VGAM174 host target gene. KIAA1755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1755 BINDING SITE, designated SEQ ID:30745, to the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, also designated SEQ ID:2885.

[11717] Another function of VGAM174 is therefore inhibition of KIAA1755 (Accession XM_028810). Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1755. LOC145474 (Accession XM_085147) is another VGAM174 host target gene. LOC145474 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145474, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145474 BINDING SITE, designated SEQ ID:37867, to the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, also designated SEQ ID:2885.

[11718] Another function of VGAM174 is therefore inhibition of LOC145474 (Accession XM_085147). Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC145474. LOC256283 (Accession XM_173105) is another VGAM174 host target gene. LOC256283 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256283 BINDING SITE, designated SEQ ID:46362, to the nucleotide sequence of VGAM174 RNA, herein designated VGAM RNA, also designated SEQ ID:2885.

[11719] Another function of VGAM174 is therefore inhibition of LOC256283 (Accession XM_173105). Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256283. LOC90593 (Accession XM_032815) is another VGAM174 host target gene. LOC90593 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90593, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90593 BINDING SITE, designated SEQ ID:31763, to the nucleotide sequence of VGAM174 RNA, herein designated

VGAM RNA, also designated SEQ ID:2885.

[11720] Another function of VGAM174 is therefore inhibition of LOC90593 (Accession XM_032815). Accordingly, utilities of VGAM174 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90593. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 175 (VGAM175) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11721] VGAM175 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM175 was detected is described hereinabove with reference to Figs. 1–8.

[11722] VGAM175 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11723] VGAM175 gene encodes a VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM175 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM175 precursor RNA is designated SEQ ID:161, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:161 is located at position 207866 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11724] VGAM175 precursor RNA folds onto itself, forming VGAM175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11725] An enzyme complex designated DICER COMPLEX, `dices` the VGAM175 folded precursor RNA into VGAM175 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM175 RNA is designated SEQ ID:2886, and is provided hereinbelow with reference to the sequence listing part.

[11726] VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM175 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11727] VGAM175 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM175 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM175 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11728] The complementary binding of VGAM175 RNA, herein designated VGAM RNA, to host target binding sites on VGAM175 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM175 host target RNA into VGAM175 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11729] It is appreciated that VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM175 host target genes. The mRNA of each one of this plurality of VGAM175 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM175 RNA, herein designated VGAM RNA, and which when bound by VGAM175 RNA causes inhibition of translation of respective one or more VGAM175 host target proteins.

[11730] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM175 gene, herein designated VGAM GENE, on one or more VGAM175 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[11731] It is yet further appreciated that a function of VGAM175 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM175 correlate with, and may be deduced from, the identity of the host target genes which VGAM175 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11732] Nucleotide sequences of the VGAM175 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM175 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM175 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM175 are further described hereinbelow with reference to Table 1.

[11733] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM175 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM175 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11734] As mentioned hereinabove with reference to Fig. 1, a function of VGAM175 gene, herein designated VGAM is inhibition of expression of VGAM175 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM175 correlate with, and may be deduced from, the identity of the target genes which VGAM175 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11735] Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM_003734) is a VGAM175 host target gene. AOC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AOC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AOC3 BINDING SITE, designated SEQ ID:9823, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11736] A function of VGAM175 is therefore inhibition of Amine Oxidase, Copper Containing 3 (vascular adhesion protein 1) (AOC3, Accession NM_003734), a gene which catalyze the oxidative conversion of amines to aldehydes in the presence of copper and quinone cofactor. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AOC3. The function of AOC3 has been established by previous studies. Zhang and McIntire (1996) cloned a novel amine oxidase, HPAO, from a human placenta cDNA library. The gene encodes a 763–amino acid polypeptide which contains a secretory signal sequence. Morris et al. (1997) cloned a partial rat cDNA which they identified as the rat homolog of HPAO. They reported that the product is a major protein on the adipocyte plasma membrane. Smith et al. (1998) studied vascular adhesion protein–1 (VAP1), a molecule expressed in endothelial cells that mediates binding of lymphocytes. These authors noted that the amino acid sequence of VAP1 was identical to that of HPAO. Expression studies revealed that the VAP1 protein has adhesive properties and also has functional monoamine oxidase activity. Northern blot analysis detected a 4.1–kb mRNA in a wide variety of human tissues.

- [11737] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [11738] Morris, N. J.; Ducret, A.; Aebersold, R.; Ross, S. A.; Keller, S. R.; Lienhard, G. E. : Membrane amine oxidase cloning and identification as a major protein in the adipocyte plasma membrane. *J. Biol. Chem.* 272: 9388–9392, 1997. ; and
- [11739] Smith, D. J.; Salmi, M.; Bono, P.; Hellman, J.; Leu, T.; Jalkanen, S. : Cloning of vascular adhesion protein 1 reveals a novel multifunctional adhesion molecule. *J. Exp. Med.* 188: 17–27.
- [11740] Further studies establishing the function and utilities of AOC3 are found in John Hopkins OMIM database record ID 603735, and in cited publications numbered 6313–631 and 5187–5188 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Bardet–Biedl Syndrome 4 (BBS4, Accession NM_033028) is another VGAM175 host target gene. BBS4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BBS4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus–

trates the complementarity of the nucleotide sequences of BBS4 BINDING SITE, designated SEQ ID:26921, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11741] Another function of VGAM175 is therefore inhibition of Bardet-Biedl Syndrome 4 (BBS4, Accession NM_033028). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BBS4. Chromosome X Open Reading Frame 6 (CXorf6, Accession NM_005491) is another VGAM175 host target gene. CXorf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXorf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf6 BINDING SITE, designated SEQ ID:11994, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11742] Another function of VGAM175 is therefore inhibition of Chromosome X Open Reading Frame 6 (CXorf6, Accession NM_005491). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with CXorf6. Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409) is another VGAM175 host target gene. DMPK BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DMPK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMPK BINDING SITE, designated SEQ ID:10663, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11743] Another function of VGAM175 is therefore inhibition of Dystrophia Myotonica-protein Kinase (DMPK, Accession NM_004409). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMPK. Milk Fat Globule-EGF Factor 8 Protein (MFGE8, Accession NM_005928) is another VGAM175 host target gene. MFGE8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MFGE8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MFGE8 BIND-

ING SITE, designated SEQ ID:12558, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11744] Another function of VGAM175 is therefore inhibition of Milk Fat Globule-EGF Factor 8 Protein (MFGE8, Accession NM_005928), a gene which links apoptotic cells to phagocytes. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFGE8. The function of MFGE8 has been established by previous studies. Stubbs et al. (1990) identified a cDNA for a mouse mammary epithelial cell surface protein, which they called milk fat globule-EGF factor 8 (MFGE8) because of its regions of sequence similarity to epidermal growth factor (EGF) and blood clotting factors VIII (OMIM Ref. No. 306700) and V (OMIM Ref. No. 227400). Larocca et al. (1991) raised monoclonal antibodies to a 46-kD human milk fat globule protein, later to be identified as the human homolog of MFGE8, and isolated a partial cDNA by immunoscreening a lambda gt11 human breast cDNA library. Collins et al. (1997) cloned the MFGE8 gene from a human infant cDNA brain library. The gene predicts a protein of 387 amino acids of which 263 (68%) are identical or conserved matches with the mouse

protein. Hanayama et al. (2002) found that MFGE8 is a factor that links apoptotic cells to phagocytes. MFGE8 specifically bound to apoptotic cells by recognizing aminophospholipids such as phosphatidylserine. MFGE8, when engaged by phospholipids, bound to cells via its RGD (arg-gly-asp) motif. It bound particularly strongly to cells expressing alpha-V-beta-3 integrin (see OMIM Ref. No. 193210). The NIH3T3 cell transformants that expressed a high level of alpha-V-beta-3 integrin engulfed apoptotic cells when MFGE8 was added. MFGE8 carrying a point mutation in the RGD motif behaved as a dominant-negative form, and inhibited the phagocytosis of apoptotic cells by peritoneal macrophages in vitro and in vivo. Hanayama et al. (2002) concluded that MFGE8 secreted from activated macrophages binds to apoptotic cells and brings them to phagocytes for engulfment.

[11745] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11746] Stubbs, J. D.; Lekutis, C.; Singer, K. L.; Bui, A.; Yuzuki, D.; Srinivasan, U.; Parry, G. : cDNA cloning of a mouse mammary epithelial cell surface protein reveals the existence of epidermal growth factor-like domains linked to factor

VIII-like sequences. Proc. Nat. Acad. Sci. 87: 8417–8421, 1990. ; and

[11747] Hanayama, R.; Tanaka, M.; Miwa, K.; Shinohara, A.; Iwamatsu, A.; Nagata, S. : Identification of a factor that links apoptotic cells to phagocytes. Nature 417: 182–187, 2002.

[11748] Further studies establishing the function and utilities of MFGE8 are found in John Hopkins OMIM database record ID 602281, and in cited publications numbered 8571–8576 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 7 (MLLT7, Accession NM_005938) is another VGAM175 host target gene. MLLT7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT7 BINDING SITE, designated SEQ ID:12575, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11749] Another function of VGAM175 is therefore inhibition of Myeloid/lymphoid Or Mixed–lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 7 (MLLT7, Accession NM_005938), a gene which is a Member of the fork–head family. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT7. The function of MLLT7 has been established by previous studies. A breakpoint in 11q23 is frequently involved in translocations underlying hematologic malignancies, especially acute leukemias. The human homolog of Drosophila 'trithorax,' symbolized MLL (OMIM Ref. No. 159555), for 'myeloid–lymphoid leukemia' or 'mixed lineage leukemia,' is located at this breakpoint. Part of the MLL gene is fused with other genes in leukemia: AF4 (OMIM Ref. No. 159557) in t(4;11)(q21;q23); ENL (OMIM Ref. No. 159556) in t(11;19)(q23;p13.3), AF9 (OMIM Ref. No. 159558) in t(9;11)(p22;q23), AF6 (OMIM Ref. No. 159559) in t(6;11)(q27;q23), and AFX in t(X;11)(q13;q23). Translocations at 11q23 result in the formation of 2 derivative chromosomes that encode chimeric transcripts. The der(11) transcript contains 5–prime MLL sequences fused to 3–prime sequences of the gene located on the partner

chromosome, whereas the other derivative chromosome contains the 5-prime sequence of the partner gene potentially fused to the 3-prime sequence of MLL. However, in 25% of patients, translocations are associated with deletions of MLL sequence that is 3-prime to the breakpoint. Thus, in these cases, a fusion transcript from the other derivative chromosome cannot be formed. In addition, analysis of complex 11q23 translocations revealed that the der(11) junction is always conserved. These data indicate that the fusion transcript encoded by the der(11) must be critical to leukemogenesis. Corral et al. (1993) found from a partial sequence of a fusion between MLL and the AFX1 gene from the X chromosome that the latter is rich in ser/pro codons, like the ENL mRNA. Corral et al. (1993) concluded that heterogeneous 11q23 abnormalities may cause attachment of ser/pro-rich segments to the N terminus of MLL, lacking the zinc finger region, and that translocations occur in early hematopoietic cells, before commitment to distinct lineages. Parry et al. (1994) cloned and sequenced the t(X;11) breakpoint region from a cell line established from an infant with acute lymphocytic leukemia. The AFX1 gene (also symbolized MLLT7) was expressed in a variety of cell types. Sequence analysis

indicated a high degree of homology between AFX1 and the forkhead family of transcription factors. The high degree of identity within the forkhead region and the lack of homology outside that region suggested to the authors that AFX1 represents a novel forkhead family member. It was predicted that a chimeric fusion protein that altered DNA binding activity would result from the translocation.

[11750] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11751] Corral, J.; Forster, A.; Thompson, S.; Lampert, F.; Kaneko, Y.; Slater, R.; Kroes, W. G.; van der Schoot, C. E.; Ludwig, W.-D.; Karpas, A.; Pocock, C.; Cotter, F.; Rabbitts, T. H. : Acute leukemias of different lineages have similar MLL gene fusions encoding related chimeric proteins resulting from chromosomal translocation. *Proc. Nat. Acad. Sci.* 90: 8538–8542, 1993. ; and

[11752] Parry, P.; Wei, Y.; Evans, G. : Cloning and characterization of the t(X;11) breakpoint from a leukemic cell line identify a new member of the forkhead gene family. *Genes Chromosomes Can.*

[11753] Further studies establishing the function and utilities of MLLT7 are found in John Hopkins OMIM database record

ID 300033, and in cited publications numbered 916 and 12194–8709 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Kinase, CAMP-dependent, Catalytic, Alpha (PRKACA, Accession NM_002730) is another VGAM175 host target gene. PRKACA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKACA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKACA BINDING SITE, designated SEQ ID:8598, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11754] Another function of VGAM175 is therefore inhibition of Protein Kinase, CAMP-dependent, Catalytic, Alpha (PRKACA, Accession NM_002730), a gene which phosphorylates target proteins on serine or threonine residues. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKACA. The function of PRKACA has been established by previous studies. Most of the effects of cAMP in the eukaryotic cell are mediated through the

phosphorylation of target proteins on serine or threonine residues by the cAMP-dependent protein kinase (EC 2.7.1.37). The inactive cAMP-dependent protein kinase is a tetramer composed of 2 regulatory and 2 catalytic subunits. The cooperative binding of 4 molecules of cAMP dissociates the enzyme in a regulatory subunit dimer and 2 free active catalytic subunits. In the human, 4 different regulatory subunits (PRKAR1A, 188830; PRKAR1B, 176911; PRKAR2A, 176910; and PRKAR2B, 176912) and 3 catalytic subunits (PRKACA; PRKACB, 176892; and PRKACG 176893) have been identified. Using PCR and Southern blot analysis, Tasken et al. (1996) assigned the PRKACA gene to chromosome 19. By 2-color fluorescence in situ hybridization, they regionalized the assignment to 19p13.1. Animal model experiments lend further support to the function of PRKACA. The intracellular second messenger cAMP affects cell physiology by directly interacting with effector molecules that include cyclic nucleotide-gated ion channels, cAMP-regulated G protein exchange factors, and cAMP-dependent protein kinases (PKA). Two catalytic subunits, C-alpha (OMIM Ref. No. PRKACA) and C-beta (OMIM Ref. No. PRKACB), are expressed in the mouse and mediate the effects of PKA. Skalhegg et al.

(2002) generated a null mutation in the major catalytic subunit of PKA, C-alpha, and observed early postnatal lethality in the majority of C-alpha knockout mice. Surprisingly, a small percentage of C-alpha knockout mice, although runted, survived to adulthood. This growth retardation was not due to decreased GH (OMIM Ref. No. 139250) production but did correlate with a reduction in IGF1 (OMIM Ref. No. 147440) mRNA in the liver and diminished production of the major urinary proteins in kidney. In these animals, compensatory increases in C-beta levels occurred in brain whereas many tissues, including skeletal muscle, heart, and sperm, contained less than 10% of the normal PKA activity. Analysis of sperm in C-alpha knockout males revealed that spermatogenesis progressed normally but that mature sperm had defective forward motility

[11755] It is appreciated that the abovementioned animal model for PRKACA is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11756] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11757] Skalhegg, B. S.; Huang, Y.; Su, T.; Idzerda, R. L.; McKnight, G. S.; Burton, K. A. : Mutation of the C-alpha subunit of PKA leads to growth retardation and sperm dysfunction. *Molec. Endocr.* 16: 630-639, 2002. ; and
- [11758] Tasken, K.; Solberg, R.; Zhao, Y.; Hansson, V.; Jahnsen, T.; Siciliano, M. J. : The gene encoding the catalytic subunit C-alpha of cAMP-dependent protein kinase (locus PRKACA) localize.
- [11759] Further studies establishing the function and utilities of PRKACA are found in John Hopkins OMIM database record ID 601639, and in cited publications numbered 6683-6684 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TEM6 (Accession NM_022748) is another VGAM175 host target gene. TEM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TEM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TEM6 BINDING SITE, designated SEQ ID:22961, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.
- [11760] Another function of VGAM175 is therefore inhibition of

TEM6 (Accession NM_022748), a gene which displays elevated expression during tumor angiogenesis. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TEM6. The function of TEM6 has been established by previous studies. Using serial analysis of gene expression (SAGE), St Croix et al. (2000) identified partial cDNAs corresponding to several tumor endothelial markers (TEMs) that displayed elevated expression during tumor angiogenesis. Among the genes they identified was TEM6. Using database searches and 5-prime RACE, Carson-Walter et al. (2001) derived sequences covering the entire TEM6 coding region, which encodes a 261-amino acid protein.

[11761] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11762] Carson-Walter, E. B.; Watkins, D. N.; Nanda, A.; Vogelstein, B.; Kinzler, K. W.; St. Croix, B. : Cell surface tumor endothelial markers are conserved in mice and humans. Cancer Res. 61: 6649-6655, 2001. ; and

[11763] St. Croix, B.; Rago, C.; Velculescu, V.; Traverso, G.; Romans, K. E.; Montgomery, E.; Lal, A.; Riggins, G. J.;

Lengauer, C.; Vogelstein, B.; Kinzler, K. W. : Genes expressed in human t.

[11764] Further studies establishing the function and utilities of TEM6 are found in John Hopkins OMIM database record ID 606825, and in cited publications numbered 689 and 6907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor AP-4 (activating enhancer binding protein 4) (TFAP4, Accession NM_003223) is another VGAM175 host target gene. TFAP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFAP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFAP4 BINDING SITE, designated SEQ ID:9224, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11765] Another function of VGAM175 is therefore inhibition of Transcription Factor AP-4 (activating enhancer binding protein 4) (TFAP4, Accession NM_003223), a gene which activates both viral and cellular genes by binding to the symmetrical dna sequence 5'-cagctg-3'. Accordingly, util-

ities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFAP4. The function of TFAP4 has been established by previous studies. Transcription factors of the basic helix-loop-helix-zipper (bHLH-Zip) family contain a basic domain, which is used for DNA binding, and HLH and Zip domains, which are used for oligomerization. Transcription factor AP4 activates both viral and cellular genes by binding to the symmetrical DNA sequence CAGCTG (Mermod et al., 1988; Hu et al., 1990). By interspecific backcross analysis, Steingrimsson et al. (1995) mapped the Tfap4 gene to mouse chromosome 16, close to the gene for sperm protamine P1 (PRM1; 182880). Since the PRM1 is located on chromosome 16p13.3 in the human, they suggested that TFAP4 is probably on human chromosome 16. The International Radiation Hybrid Mapping Consortium mapped the TFAP4 gene to chromosome 16p13 (sts-S73885).

[11766] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11767] Hu, Y.-F.; Luscher, B.; Admon, A.; Mermod, N.; Tjian, R. : Transcription factor AP-4 contains multiple dimerization

domains that regulate dimer specificity. Genes Dev. 4: 1741–1752, 1990. ; and

[11768] Steingrimsson, E.; Sawadogo, M.; Gilbert, D. J.; Zervos, A. S.; Brent, R.; Blonar, M. A.; Fisher, D. E.; Copeland, N. G.; Jenkins, N. A. : Murine chromosomal location of five bHLH–Zip tr.

[11769] Further studies establishing the function and utilities of TFAP4 are found in John Hopkins OMIM database record ID 600743, and in cited publications numbered 7581–758 and 12617 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tumor Necrosis Factor (TNF superfamily, member 2) (TNF, Accession XM_165823) is another VGAM175 host target gene. TNF BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TNF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNF BINDING SITE, designated SEQ ID:43771, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11770] Another function of VGAM175 is therefore inhibition of Tumor Necrosis Factor (TNF superfamily, member 2) (TNF,

Accession XM_165823), a gene which mediates proinflammatory responses and apoptosis. Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNF. The function of TNF has been established by previous studies. Ruuls and Sedgwick (1999) reviewed the problem of unlinking TNF biology from that of the MHC. Dysregulation and, in particular, overproduction of TNF have been implicated in a variety of human diseases, including sepsis, cerebral malaria, and autoimmune diseases such as multiple sclerosis (OMIM Ref. No. 126200), rheumatoid arthritis, systemic lupus erythematosus (OMIM Ref. No. 152700), and Crohn disease (see OMIM Ref. No. 266600), as well as cancer. Susceptibility to many of these diseases is thought to have a genetic basis, and the TNF gene is considered a candidate predisposing gene. However, unraveling the importance of genetic variation in the TNF gene to disease susceptibility or severity is complicated by its location within the MHC, a highly polymorphic region that encodes numerous genes involved in immunologic responses. Ruuls and Sedgwick (1999) reviewed studies that had analyzed the contribution of TNF and related genes to susceptibility to human disease, and they dis-

cussed how the presence of the TNF gene within the MHC may potentially complicate the interpretation of studies in animal models in which the TNF gene is experimentally manipulated. Animal model experiments lend further support to the function of TNF. Bruce et al. (1996) used targeted gene disruption to generate mice lacking either the p55 or the p75 TNF receptors; mice lacking both p55 and p75 were generated from crosses of the singly deficient mice. The TNFR-deficient (TNFR-KO) mice exhibited no overt phenotype under unchallenged conditions. Bruce et al. (1996) reported that damage to neurons caused by focal cerebral ischemia and epileptic seizures was exacerbated in the TNFR-KO mice, indicating that TNF serves a neuroprotective function. Their studies indicated that TNF protects neurons by stimulating antioxidative pathways. Injury-induced microglial activation was suppressed in TNFR-KO mice. They concluded that drugs which target TNF signaling pathways may prove beneficial in treating stroke or traumatic brain injury.

[11771] It is appreciated that the abovementioned animal model for TNF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[11772] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11773] Ruuls, S. R.; Sedgwick, J. D. : Unlinking tumor necrosis factor biology from the major histocompatibility complex: lessons from human genetics and animal models. Am. J. Hum. Genet. 65: 294–301, 1999. ; and

[11774] Bruce, A. J.; Boling, W.; Kindy, M. S.; Peschon, J.; Kraemer, P. J.; Carpenter, M. K.; Holtsberg, F. W.; Mattson, M. P. : Altered neuronal and microglial responses to excitotoxic and is.

[11775] Further studies establishing the function and utilities of TNF are found in John Hopkins OMIM database record ID 191160, and in cited publications numbered 663, 9569–9574, 451, 9575, 12122–9577, 3684, 12303–9579, 3051, 9580–9582, 2981, 9583–9584, 9798, 10523–10539, 10542, 12143–10541, 10543–10544, 12305–1054 and 10567 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM_029741) is another VGAM175 host target gene. C20orf130 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by C20orf130, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf130 BINDING SITE, designated SEQ ID:30936, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11776] Another function of VGAM175 is therefore inhibition of Chromosome 20 Open Reading Frame 130 (C20orf130, Accession XM_029741). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf130. DKFZP434K1772 (Accession XM_041936) is another VGAM175 host target gene. DKFZP434K1772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434K1772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K1772 BINDING SITE, designated SEQ ID:33630, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11777] Another function of VGAM175 is therefore inhibition of DKFZP434K1772 (Accession XM_041936). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434K1772. DKFZP564F0522 (Accession XM_043885) is another VGAM175 host target gene. DKFZP564F0522 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564F0522, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564F0522 BINDING SITE, designated SEQ ID:34041, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11778] Another function of VGAM175 is therefore inhibition of DKFZP564F0522 (Accession XM_043885). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564F0522. FLJ10661 (Accession NM_018172) is another VGAM175 host target gene. FLJ10661 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10661, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10661 BINDING SITE, designated SEQ ID:19995, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11779] Another function of VGAM175 is therefore inhibition of FLJ10661 (Accession NM_018172). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10661. FLJ14950 (Accession NM_032865) is another VGAM175 host target gene. FLJ14950 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14950 BINDING SITE, designated SEQ ID:26676, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11780] Another function of VGAM175 is therefore inhibition of FLJ14950 (Accession NM_032865). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ14950. FLJ20847 (Accession XM_170677) is another VGAM175 host target gene. FLJ20847 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20847, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20847 BINDING SITE, designated SEQ ID:45458, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11781] Another function of VGAM175 is therefore inhibition of FLJ20847 (Accession XM_170677). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20847. KIAA1100 (Accession NM_014901) is another VGAM175 host target gene. KIAA1100 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1100 BINDING SITE, designated SEQ ID:17084, to the nucleotide sequence of

VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11782] Another function of VGAM175 is therefore inhibition of KIAA1100 (Accession NM_014901). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1100. Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971) is another VGAM175 host target gene. MRPL20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL20 BINDING SITE, designated SEQ ID:19696, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11783] Another function of VGAM175 is therefore inhibition of Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL20. PP1628 (Accession NM_025201) is another VGAM175 host target gene.

PP1628 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PP1628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1628 BINDING SITE, designated SEQ ID:24856, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11784] Another function of VGAM175 is therefore inhibition of PP1628 (Accession NM_025201). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1628. PRKRI (Accession NM_006260) is another VGAM175 host target gene. PRKRI BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRKRI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKRI BINDING SITE, designated SEQ ID:12943, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11785] Another function of VGAM175 is therefore inhibition of PRKRI (Accession NM_006260). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKRI. Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6A (SEMA6A, Accession NM_020796) is another VGAM175 host target gene. SEMA6A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEMA6A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEMA6A BINDING SITE, designated SEQ ID:21880, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11786] Another function of VGAM175 is therefore inhibition of Sema Domain, Transmembrane Domain (TM), and Cytoplasmic Domain, (semaphorin) 6A (SEMA6A, Accession NM_020796). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEMA6A. Sp2 Transcription Factor (SP2, Accession NM_003110) is another VGAM175

host target gene. SP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP2 BINDING SITE, designated SEQ ID:9080, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11787] Another function of VGAM175 is therefore inhibition of Sp2 Transcription Factor (SP2, Accession NM_003110). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP2. TGFB1-induced Anti-apoptotic Factor 1 (TIAF1, Accession NM_078471) is another VGAM175 host target gene. TIAF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIAF1 BINDING SITE, designated SEQ ID:27797, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2886.

[11788] Another function of VGAM175 is therefore inhibition of TGF β 1-induced Anti-apoptotic Factor 1 (TIAF1, Accession NM_078471). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIAF1. LOC124930 (Accession XM_058867) is another VGAM175 host target gene. LOC124930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124930 BINDING SITE, designated SEQ ID:36766, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11789] Another function of VGAM175 is therefore inhibition of LOC124930 (Accession XM_058867). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124930. LOC145719 (Accession XM_096848) is another VGAM175 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40573, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11790] Another function of VGAM175 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM175 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40564, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11791] Another function of VGAM175 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities

of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145720. LOC145725 (Accession XM_085211) is another VGAM175 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37947, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11792] Another function of VGAM175 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM175 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC145732 BINDING SITE, designated SEQ ID:37956, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11793] Another function of VGAM175 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC146562 (Accession NM_139170) is another VGAM175 host target gene. LOC146562 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146562, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146562 BINDING SITE, designated SEQ ID:29178, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11794] Another function of VGAM175 is therefore inhibition of LOC146562 (Accession NM_139170). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146562. LOC151878 (Accession XM_087329) is another VGAM175 host target gene. LOC151878 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC151878, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151878 BINDING SITE, designated SEQ ID:39172, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11795] Another function of VGAM175 is therefore inhibition of LOC151878 (Accession XM_087329). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151878. LOC197419 (Accession XM_117035) is another VGAM175 host target gene. LOC197419 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197419, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197419 BINDING SITE, designated SEQ ID:43209, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11796] Another function of VGAM175 is therefore inhibition of

LOC197419 (Accession XM_117035). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197419. LOC257551 (Accession XM_175158) is another VGAM175 host target gene. LOC257551 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257551, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257551 BINDING SITE, designated SEQ ID:46645, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11797] Another function of VGAM175 is therefore inhibition of LOC257551 (Accession XM_175158). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257551. LOC257601 (Accession XM_175231) is another VGAM175 host target gene. LOC257601 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257601, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC257601 BINDING SITE, designated SEQ ID:46696, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11798] Another function of VGAM175 is therefore inhibition of LOC257601 (Accession XM_175231). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257601. LOC91300 (Accession XM_170568) is another VGAM175 host target gene. LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC91300, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91300 BINDING SITE1 and LOC91300 BINDING SITE2, designated SEQ ID:45386 and SEQ ID:29005 respectively, to the nucleotide sequence of VGAM175 RNA, herein designated VGAM RNA, also designated SEQ ID:2886.

[11799] Another function of VGAM175 is therefore inhibition of LOC91300 (Accession XM_170568). Accordingly, utilities of VGAM175 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC91300. MAD2 Mitotic Arrest Deficient-like 1 (yeast) (MAD2L1, Accession NM_002358) is another VGAM176 host target gene. MAD2L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAD2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAD2L1 BINDING SITE, designated SEQ ID:8170, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11800] Another function of VGAM176 is therefore inhibition of MAD2 Mitotic Arrest Deficient-like 1 (yeast) (MAD2L1, Accession NM_002358), a gene which may monitor the completeness of the spindle-kinetochore attachment. delays the onset of anaphase when this process is not complete. Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAD2L1. The function of MAD2L1 has been established by previous studies. Using a yeast 2-hybrid analysis with the cytoplasmic tails of several a disintegrin and metalloproteinase domain (ADAM) pro-

teins as bait, Nelson et al. (1999) found that MAD2L1 interacts strongly with TACE (ADAM17; 603639) but not with ADAM9 (OMIM Ref. No. 602713), which interacts with MAD2L2, or with other ADAMs tested. Further binding analyses defined a 35-amino acid stretch of TACE containing a proline-rich SH3-ligand domain (OMIM Ref. No. PXPXXP) as the interaction site for MAD2L1. Luo et al. (2002) showed that RNA interference-mediated suppression of MAD1 (OMIM Ref. No. 602686) function in mammalian cells caused loss of MAD2 kinetochore localization and impairment of the spindle checkpoint. MAD1 and CDC20 (OMIM Ref. No. 603618) contain MAD2-binding motifs that share a common consensus, and the authors identified a class of MAD2-binding peptides (MBPs) with a similar consensus. Binding of one of these ligands, MBP1, triggered an extensive rearrangement of the tertiary structure of MAD2. MAD2 also underwent a similar striking structural change upon binding to a MAD1 or CDC20 binding motif peptide. These data suggested that, upon checkpoint activation, MAD1 recruits MAD2 to unattached kinetochores and may promote binding of MAD2 to CDC20. Animal model experiments lend further support to the function of MAD2L1. The initiation of chromosome

segregation at anaphase is linked by the spindle assembly checkpoint to the completion of chromosome-microtubule attachment during metaphase. To determine the function of the Mad2 protein during normal cell division, Dobles et al. (2000) knocked out the Mad2 gene in mice. They found that embryonic cells lacking Mad2 at embryonic day 5.5, like *mad2* yeast, grew normally but were unable to arrest in response to spindle disruption. At embryonic day 6.5, the cells of the epiblast began rapid cell division, and the absence of a checkpoint resulted in widespread chromosome missegregation and apoptosis. In contrast, the postmitotic trophoblast giant cells survived without Mad2. Thus, the spindle assembly checkpoint is required for accurate chromosome segregation in mitotic mouse cells and for embryonic viability, even in the absence of spindle damage. Shonn et al. (2000) characterized the spindle checkpoint in meiosis of *S. cerevisiae* by comparing wildtype and *mad2*-deficient yeast. In the absence of the checkpoint, the frequency of meiosis I missegregation increased with increasing chromosome length, reaching 19% for the longest chromosome. Meiosis I nondisjunction in spindle checkpoint mutants could be prevented by delaying the onset of anaphase. In a recom-

binant-defective mutant, the checkpoint delayed the biochemical events of anaphase I, suggesting that chromosomes that are attached to microtubules but are not under tension can activate the spindle checkpoint. Spindle checkpoint mutants reduced the accuracy of chromosome segregation in meiosis I much more than that in meiosis II, suggesting that checkpoint defects may contribute to Down syndrome (OMIM Ref. No. 190685). Shonn et al. (2000) showed that the budding yeast spindle checkpoint, which is largely dispensable in wildtype mitosis, plays a critical role in meiotic chromosome segregation. They suggested that the difference may reflect the different chromosome linkages in mitosis and meiosis I. In mitosis, sister chromatid cohesion forces sister kinetochores to face opposite spindle poles. In meiosis I, homologs are linked at sites of recombination that can be far from the kinetochores, creating a floppy linkage. If the nearest recombination event is further from the centromere on long chromosomes, this idea may explain why long chromosomes preferentially nondisjoin in checkpoint-defective cells. Michel et al. (2001) reported that deletion of one MAD2 allele results in a defective mitotic checkpoint in both human cancer cells and murine primary embryonic

fibroblasts. Checkpoint-defective cells show premature sister chromatid separation in the presence of spindle inhibitors and an elevated rate of chromosome missegregation events in the absence of these agents. Furthermore, Mad2 +/– mice develop lung tumors at high rates after long latencies, implicating defects in the mitotic checkpoint in tumorigenesis

[11801] It is appreciated that the abovementioned animal model for MAD2L1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11802] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11803] Michel, L. S.; Liberal, V.; Chatterjee, A.; Kirchwegger, R.; Pasche, B.; Gerald, W.; Dobles, M.; Sorger, P. K.; Murty, V. V. S.; Benezra, R. : MAD2 haplo-insufficiency causes premature anaphase and chromosome instability in mammalian cells. Nature 409: 355–359, 2001. ; and

[11804] Luo, X.; Tang, Z.; Rizo, J.; Yu, H. : The Mad2 spindle checkpoint protein undergoes similar major conformational changes upon binding to either Mad1 or Cdc20. Molec. Cell 9: 59–71, 2002.

[11805] Further studies establishing the function and utilities of MAD2L1 are found in John Hopkins OMIM database record ID 601467, and in cited publications numbered 2758–2768 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Macrophage Scavenger Receptor 1 (MSR1, Accession NM_138715) is another VGAM176 host target gene. MSR1 BINDING SITE1 and MSR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MSR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSR1 BINDING SITE1 and MSR1 BINDING SITE2, designated SEQ ID:28960 and SEQ ID:28962 respectively, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11806] Another function of VGAM176 is therefore inhibition of Macrophage Scavenger Receptor 1 (MSR1, Accession NM_138715), a gene which plays a role in endocytosis of macromolecules. Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSR1. The function of

MSR1 has been established by previous studies. Deletions on 8p23–p22 in prostate cancer cells (Latil and Lidereau, 1998) and linkage studies in families affected with hereditary prostate cancer (Xu et al., 2001) have implicated this region in the development of prostate cancer. The MSR1 gene is located at 8p22 and functions in several processes proposed to be relevant to prostate carcinogenesis. In studies of families affected with hereditary prostate cancer, Xu et al. (2002) identified 6 missense mutations and 1 nonsense mutation in the MSR1 gene. A family-based linkage and association test indicated that these mutations cosegregate with prostate cancer ($P = 0.0007$). In addition, among men of European descent, MSR1 mutations were detected in 4.4% of individuals affected with nonhereditary prostate cancer as compared with 0.8% of unaffected men ($P = 0.009$). Among African American men, these values were 12.5% and 1.8%, respectively ($P = 0.01$). These results showed that MSR1 may be important in susceptibility to prostate cancer in men of both African American and European descent.

[11807] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [11808] Emi, M.; Asaoka, H.; Matsumoto, A.; Itakura, H.; Kurihara, Y.; Wada, Y.; Kanamori, H.; Yazaki, Y.; Takahashi, E.; Lepert, M.; Lalouel, J.-M.; Kodama, T.; Mukai, T. : Structure, organization, and chromosomal mapping of the human macrophage scavenger receptor gene. *J. Biol. Chem.* 268: 2120–2125, 1993. ; and
- [11809] Latil, A.; Lidereau, R. : Genetic aspects of prostate cancer. *Virchows Arch.* 432: 389–406, 1998.
- [11810] Further studies establishing the function and utilities of MSR1 are found in John Hopkins OMIM database record ID 153622, and in cited publications numbered 11661–11665 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite Motif-containing 39 (TRIM39, Accession NM_021253) is another VGAM176 host target gene. TRIM39 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRIM39, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM39 BINDING SITE, designated SEQ ID:22225, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ

ID:2887.

[11811] Another function of VGAM176 is therefore inhibition of Tripartite Motif-containing 39 (TRIM39, Accession NM_021253). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM39. COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM_022730) is another VGAM176 host target gene. COPS7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COPS7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COPS7B BINDING SITE, designated SEQ ID:22930, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11812] Another function of VGAM176 is therefore inhibition of COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM_022730). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COPS7B. KIAA1229 (Accession XM_030665)

is another VGAM176 host target gene. KIAA1229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1229 BINDING SITE, designated SEQ ID:31095, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11813] Another function of VGAM176 is therefore inhibition of KIAA1229 (Accession XM_030665). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1229. NRF (Accession NM_017544) is another VGAM176 host target gene. NRF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRF BINDING SITE, designated SEQ ID:18983, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11814] Another function of VGAM176 is therefore inhibition of NRF (Accession NM_017544). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRF. UBX Domain Containing 2 (UBXD2, Accession XM_043196) is another VGAM176 host target gene. UBXD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UBXD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBXD2 BINDING SITE, designated SEQ ID:33914, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11815] Another function of VGAM176 is therefore inhibition of UBX Domain Containing 2 (UBXD2, Accession XM_043196). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBXD2. LOC115219 (Accession XM_055499) is another VGAM176 host target gene. LOC115219 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC115219, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115219 BINDING SITE, designated SEQ ID:36279, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11816] Another function of VGAM176 is therefore inhibition of LOC115219 (Accession XM_055499). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115219. LOC158187 (Accession XM_098892) is another VGAM176 host target gene. LOC158187 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158187 BINDING SITE, designated SEQ ID:41921, to the nucleotide sequence of VGAM176 RNA, herein designated VGAM RNA, also designated SEQ ID:2887.

[11817] Another function of VGAM176 is therefore inhibition of LOC158187 (Accession XM_098892). Accordingly, utilities of VGAM176 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC158187. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 177 (VGAM177) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[11818] VGAM177 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM177 was detected is described hereinabove with reference to Figs. 1–8.

[11819] VGAM177 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[11820] VGAM177 gene encodes a VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM177 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM177 precursor RNA is designated SEQ

ID:163, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:163 is located at position 117656 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11821] VGAM177 precursor RNA folds onto itself, forming VGAM177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11822] An enzyme complex designated DICER COMPLEX, `dices` the VGAM177 folded precursor RNA into VGAM177 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 59%) nucleotide sequence of VGAM177 RNA is designated SEQ ID:2888, and

is provided hereinbelow with reference to the sequence listing part.

[11823] VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM177 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[11824] VGAM177 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM177 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM177 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11825] The complementary binding of VGAM177 RNA, herein designated VGAM RNA, to host target binding sites on VGAM177 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM177 host target RNA into VGAM177 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11826] It is appreciated that VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM177 host target genes. The mRNA of each one of this plurality of VGAM177 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM177 RNA, herein designated VGAM RNA, and which when bound by VGAM177 RNA causes inhibition of translation of respective one or more VGAM177 host target proteins.

[11827] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM177 gene, herein designated VGAM GENE, on one or more VGAM177 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11828] It is yet further appreciated that a function of VGAM177 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM177 correlate with, and may be deduced from, the identity of the host target genes which VGAM177 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11829] Nucleotide sequences of the VGAM177 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM177 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM177 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM177 are further described hereinbelow with reference to Table 1.

[11830] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM177 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM177 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[11831] As mentioned hereinabove with reference to Fig. 1, a function of VGAM177 gene, herein designated VGAM is inhibition of expression of VGAM177 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM177 correlate with, and may be deduced from, the identity of the target genes which VGAM177 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11832] Cytochrome C Oxidase Subunit VIIa Polypeptide 1 (muscle) (COX7A1, Accession NM_001864) is a VGAM177 host target gene. COX7A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by COX7A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX7A1 BINDING SITE, designated SEQ ID:7602, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

[11833] A function of VGAM177 is therefore inhibition of Cytochrome C Oxidase Subunit VIIa Polypeptide 1 (muscle) (COX7A1, Accession NM_001864), a gene which is one of the nuclear-coded polypeptide chains of cytochrome c

oxidase. Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX7A1. The function of COX7A1 has been established by previous studies. Cytochrome c oxidase (COX; EC 1.9.3.1), the last component of the mitochondrial respiratory chain, catalyzes the transfer of electrons from reduced cytochrome c to molecular oxygen. In mammals, the apoprotein is composed of 3 large catalytic subunits, encoded by the mitochondrial genome (516030, 516040, and 516050), and by 10 smaller, nuclear-encoded subunits which may play a regulatory role. Subunit VIIa of mammalian COX exists in at least 2 isoforms, liver (L) and muscle (M). Arnaudo et al. (1992) isolated a full-length cDNA encoding the muscle isoform. The deduced polypeptide shares 78% identity with the bovine muscle form but only 63% identity with the human liver isoform. Northern blot analysis of primate tissues demonstrated that mRNA for the muscle form is present only in muscle tissues; in contrast, liver mRNA is present in both muscle and nonmuscle tissues. Southern blot analysis of human/rodent cell hybrid genomic DNA indicated that the muscle form is encoded by a single locus, designated COX7A1, on chromosome 19; in contrast,

cDNA probes for the liver isoform hybridized fragments from 2 loci, one on chromosome 4 (COX7A2; 123996) and the other on chromosome 14 (COX7A3; 123997 Fabrizio et al. (1989) reported the sequence of the human COX7A1 gene. Wolz et al. (1997) described the genomic sequence and organization of the human COX7A1 gene and compared it with its bovine homolog. The coding region of the gene extends over 1.45 kb of genomic sequence and is organized into 4 exons. Intron-exon boundaries are well conserved between cattle and humans. Although COX7A1 is a gene for a tissue-specific isoform, it has some features of a housekeeping gene: it is located in a CpG island, like its bovine homolog, and no TATA or CCAAT boxes are found in the 5-prime flanking sequence

[11834] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11835] Arnaudo, E.; Hirano, M.; Seelan, R. S.; Milatovich, A.; Hsieh, C.-L.; Fabrizio, G. M.; Grossman, L. I.; Francke, U.; Schon, E. A. : Tissue-specific expression and chromosome assignment of genes specifying two isoforms of subunit VIIa of human cytochrome c oxidase. Gene 119: 299-305, 1992. ; and

[11836] Fabrizi, G. M.; Rizzuto, R.; Nakase, H.; Mita, S.; Lomax, M. I.; Grossman, L. I.; Schon, E. A. : Sequence of a cDNA specifying subunit VIIa of human cytochrome c oxidase. Nucleic Acids R.

[11837] Further studies establishing the function and utilities of COX7A1 are found in John Hopkins OMIM database record ID 123995, and in cited publications numbered 87 and 3410–3411 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DNA (cytosine–5–)-methyltransferase 2 (DNMT2, Accession NM_004412) is another VGAM177 host target gene. DNMT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DNMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT2 BINDING SITE, designated SEQ ID:10669, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

[11838] Another function of VGAM177 is therefore inhibition of DNA (cytosine–5–)-methyltransferase 2 (DNMT2, Accession NM_004412), a gene which may mark specific se–

quences in the genome . Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT2. The function of DNMT2 has been established by previous studies. Trace levels of 5-methylcytosine persist in the DNA of mouse embryonic stem cells that are homozygous for null mutations in Dnmt1 (OMIM Ref. No. 126375). Yoder and Bestor (1998) showed that this residual 5-methylcytosine may be the product of a second DNA methyltransferase, Dnmt2. Dnmt2 contains all the sequence motifs diagnostic of DNA (cytosine-5)-methyltransferases but appears to lack the large N-terminal regulatory domain common to other eukaryotic methyltransferases. It is more similar to a putative DNA methyltransferase of the fission yeast *Schizosaccharomyces pombe* than to Dnmt1. Dnmt2 produces multiple mRNA species that are present at low levels in all tissues of human and mouse and is not restricted to those cell types known to be active in de novo methylation. Yoder and Bestor (1998) mapped the human DNMT2 gene to 10p14-p12 in a panel of radiation hybrids. By fluorescence in situ hybridization, Vilain et al. (1998) assigned the DNMT2 gene to 10p15.1.

[11839] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11840] Vilain, A.; Apiou, F.; Dutrillaux, B.; Malfoy, B. : Assignment of candidate DNA methyltransferase gene (DNMT2) to human chromosome band 10p15.1 by in situ hybridization. Cytogenet. Cell Genet. 82: 120 only, 1998. ; and

[11841] Yoder, J. A.; Bestor, T. H. : A candidate mammalian DNA methyltransferase related to pmt1p of fission yeast. Hum. Molec. Genet. 7: 279–284, 1998.

[11842] Further studies establishing the function and utilities of DNMT2 are found in John Hopkins OMIM database record ID 602478, and in cited publications numbered 7961–7962 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072) is another VGAM177 host target gene. C1QR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C1QR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QR1 BINDING SITE,

designated SEQ ID:14338, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

[11843] Another function of VGAM177 is therefore inhibition of Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072). Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QR1. FLJ23511 (Accession NM_032239) is another VGAM177 host target gene. FLJ23511 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23511 BINDING SITE, designated SEQ ID:25965, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

[11844] Another function of VGAM177 is therefore inhibition of FLJ23511 (Accession NM_032239). Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23511. KIAA0447 (Accession XM_049733) is another VGAM177

host target gene. KIAA0447 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35491, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

[11845] Another function of VGAM177 is therefore inhibition of KIAA0447 (Accession XM_049733). Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. MSTP032 (Accession NM_025226) is another VGAM177 host target gene. MSTP032 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MSTP032, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSTP032 BINDING SITE, designated SEQ ID:24906, to the nucleotide sequence of VGAM177 RNA, herein designated VGAM RNA, also designated SEQ ID:2888.

- [11846] Another function of VGAM177 is therefore inhibition of MSTP032 (Accession NM_025226). Accordingly, utilities of VGAM177 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSTP032. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 178 (VGAM178) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [11847] VGAM178 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM178 was detected is described hereinabove with reference to Figs. 1–8.
- [11848] VGAM178 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [11849] VGAM178 gene encodes a VGAM178 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM178 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM178 precursor RNA is designated SEQ ID:164, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:164 is located at position 152069 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[11850] VGAM178 precursor RNA folds onto itself, forming VGAM178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[11851] An enzyme complex designated DICER COMPLEX, `dices` the VGAM178 folded precursor RNA into VGAM178 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 60%) nucleotide sequence of VGAM178 RNA is designated SEQ ID:2889, and is provided hereinbelow with reference to the sequence listing part.

[11852] VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM178 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[11853] VGAM178 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM178 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM178 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[11854] The complementary binding of VGAM178 RNA, herein designated VGAM RNA, to host target binding sites on VGAM178 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM178 host target RNA into VGAM178 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[11855] It is appreciated that VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM178 host target genes. The mRNA of each one of this plurality of VGAM178 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM178 RNA, herein designated VGAM RNA, and which when bound by VGAM178 RNA causes inhibition of translation of respective one or more VGAM178 host target proteins.

[11856] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM178 gene, herein designated VGAM GENE, on one or more VGAM178 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[11857] It is yet further appreciated that a function of VGAM178 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM178 correlate with, and may be deduced from, the identity of the host target genes which VGAM178 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[11858] Nucleotide sequences of the VGAM178 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM178 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM178 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM178 are further described hereinbelow with reference to Table 1.

[11859] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM178 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM178 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[11860] As mentioned hereinabove with reference to Fig. 1, a function of VGAM178 gene, herein designated VGAM is inhibition of expression of VGAM178 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM178 correlate with, and may be deduced from, the identity of the target genes which VGAM178 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[11861] B-cell CLL/lymphoma 7A (BCL7A, Accession NM_020993) is a VGAM178 host target gene. BCL7A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7A BINDING SITE, designated SEQ ID:21990, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11862] A function of VGAM178 is therefore inhibition of B-cell CLL/lymphoma 7A (BCL7A, Accession NM_020993). Accordingly, utilities of VGAM178 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with BCL7A. Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM_000723) is another VGAM178 host target gene. CACNB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNB1 BINDING SITE, designated SEQ ID:6384, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11863] Another function of VGAM178 is therefore inhibition of Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM_000723), a gene which may not only play an important role in the transport/insertion of the alpha-1S subunit into the membrane. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNB1. The function of CACNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM114. Dual-specificity tyrosine-

(Y)–phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395) is another VGAM178 host target gene. DYRK1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DYRK1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE, designated SEQ ID:28161, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11864] Another function of VGAM178 is therefore inhibition of Dual–specificity tyrosine–(Y)–phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_101395), a gene which regulates cell proliferation and may be involved in brain development . Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42.ELK1, Member of ETS Oncogene Family (ELK1, Accession NM_005229) is another VGAM178 host target

gene. ELK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELK1 BINDING SITE, designated SEQ ID:11729, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11865] Another function of VGAM178 is therefore inhibition of ELK1, Member of ETS Oncogene Family (ELK1, Accession NM_005229), a gene which stimulates transcription. can form a ternary complex with the serum response factor and the ets and srf motifs of the fos serum response element. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELK1. The function of ELK1 has been established by previous studies. Rao et al. (1989) identified 2 new members of the ETS (164720, 164740) oncogene superfamily, ELK1 and ELK2. The ELK or related sequences appear to be transcriptionally active in testis and lung. By analysis of somatic cell hybrids and in situ hybridization, Rao et al. (1989) mapped the ELK1 gene to Xp11.2 and the ELK2 gene to 14q32.3. The former is near

the translocation breakpoint seen in t(X;18)(p11.2;q11.2), which is characteristic of synovial sarcoma; the latter is near the 14q32 breakpoint seen in ataxia–telangiectasia and other T–cell malignancies. Janz et al. (1994) used fluorescence in situ hybridization and a panel of tumor–derived somatic cell hybrids to assign the ELK1 gene to Xp11.4–p11.2, distal to the OATL1 region (OMIM Ref. No. 311240). Tamai et al. (1995) used interspecific backcross mice to map the Elk gene to the mouse X chromosome. Giovane et al. (1995) mapped ELK1 to human Xp11.2–p11.1 and to mouse XA1–A3 by in situ hybridization. Yamauchi et al. (1999) found by sequence analysis that the ELK2 locus on 14q32.2 that was identified by Rao et al. (1989) is actually a processed pseudogene (OMIM Ref. No. ELK2P1) of ELK1.

[11866] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11867] Tamai, Y.; Taketo, M.; Nozaki, M.; Seldin, M. F. : Mouse Elk oncogene maps to chromosome X and a novel Elk oncogene (Elk3) maps to chromosome 10. Genomics 26: 414–416, 1995. ; and

[11868] Yamauchi, T.; Toko, M.; Suga, M.; Hatakeyama, T.; Isobe,

M. : Structural organization of the human Elk1 gene and its processed pseudogene Elk2. DNA Res. 6: 21–27, 1999.

[11869] Further studies establishing the function and utilities of ELK1 are found in John Hopkins OMIM database record ID 311040, and in cited publications numbered 8627–8631 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM_004458) is another VGAM178 host target gene. FACL4 BINDING SITE1 and FACL4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FACL4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FACL4 BINDING SITE1 and FACL4 BINDING SITE2, designated SEQ ID:10762 and SEQ ID:23252 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11870] Another function of VGAM178 is therefore inhibition of Fatty-acid-Coenzyme A Ligase, Long-chain 4 (FACL4, Accession NM_004458). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with FACL4. H1 Histone Family, Member 0 (H1F0, Accession NM_005318) is another VGAM178 host target gene. H1F0 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H1F0, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H1F0 BINDING SITE, designated SEQ ID:11794, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11871] Another function of VGAM178 is therefore inhibition of H1 Histone Family, Member 0 (H1F0, Accession NM_005318), a gene which is necessary for the condensation of nucleosome chains into higher order structures. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H1F0. The function of H1F0 has been established by previous studies. Histones are basic nuclear proteins that are responsible for the nucleosome structure within the chromosomal fiber in eukaryotes. See 142711. Doenecke and Tonjes (1986) cloned the human H1(0) gene. By PCR analysis of chromosomal DNA from a panel of human/ro-

dent somatic cell hybrids, Albig et al. (1993) demonstrated that the H1(0) subtype maps to chromosome 22. By fluorescence in situ hybridization, they further localized the gene to 22q13.1.

[11872] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11873] Albig, W.; Drabent, B.; Kunz, J.; Kalff-Suske, M.; Grzeschik, K.-H.; Doenecke, D. : All known human H1 histone genes except the H1(0) gene are clustered on chromosome 6. Genomics 16: 649-654, 1993. ; and

[11874] Doenecke, D.; Tonjes, R. : Differential distribution of lysine and arginine residues in the closely related histones H1 and H5. Analysis of a human H1 gene. J. Molec. Biol. 187: 461-464.

[11875] Further studies establishing the function and utilities of H1F0 are found in John Hopkins OMIM database record ID 142708, and in cited publications numbered 2672 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo Box B9 (HOXB9, Accession NM_024017) is another VGAM178 host target gene. HOXB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

HOXB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXB9 BINDING SITE, designated SEQ ID:23445, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11876] Another function of VGAM178 is therefore inhibition of Homeo Box B9 (HOXB9, Accession NM_024017). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXB9. Interleukin 11 (IL11, Accession NM_000641) is another VGAM178 host target gene. IL11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL11 BINDING SITE, designated SEQ ID:6278, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11877] Another function of VGAM178 is therefore inhibition of Interleukin 11 (IL11, Accession NM_000641), a gene which

stimulates the proliferation of hematopoietic stem cells and megakaryocyte progenitor cells and induces megakaryocyte maturation. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL11. The function of IL11 has been established by previous studies. Paul et al. (1990) identified and cloned the gene for a new stromal cell-derived lymphopoietic and hematopoietic cytokine which they called interleukin-11. The cDNA indicated a single reading frame of 597 nucleotides encoding a predicted 199-amino acid polypeptide. The IL11 produced in COS-1 cells showed an apparent molecular mass of about 23 kD. McKinley et al. (1992) determined that the genomic sequence is 7 kb long and consists of 5 exons and 4 introns. Biologic characterization indicated that in addition to stimulating plasmacytoma proliferation, IL11 stimulates T-cell-dependent development of immunoglobulin-producing B cells and collaborates with IL3 in supporting murine megakaryocyte colony formation (Paul et al., 1990). Du and Williams (1994) reviewed the pleiotropic effects of IL11 on hematopoietic cells. Yang-Feng et al. (1991) demonstrated by in situ hybridization that a cDNA for IL11 maps to 19q13.3-q13.4. Since

translocations involving 19q13 occur in patients with acute lymphocytic leukemia, the IL11 gene may be implicated. Du and Williams (1997) reviewed the molecular, cell biologic, and clinical aspects of interleukin-11.

[11878] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11879] Du, X.; Williams, D. A. : Interleukin-11: review of molecular, cell biology, and clinical use. Blood 89: 3897-3908, 1997. ; and

[11880] Du, X. X.; Williams, D. A. : Interleukin-11: a multifunctional growth factor derived from the hematopoietic microenvironment. Blood 83: 2023-2030, 1994.

[11881] Further studies establishing the function and utilities of IL11 are found in John Hopkins OMIM database record ID 147681, and in cited publications numbered 682-686 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450) is another VGAM178 host target gene. KLHL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL3 BINDING SITE, designated SEQ ID:42266, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11882] Another function of VGAM178 is therefore inhibition of Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL3. MAD, Mothers Against Decapentaplegic Homolog 3 (Drosophila) (MADH3, Accession NM_005902) is another VGAM178 host target gene. MADH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MADH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH3 BINDING SITE, designated SEQ ID:12522, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11883] Another function of VGAM178 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog 3

(Drosophila) (MADH3, Accession NM_005902), a gene which affects transcription in response to TGF-beta signaling pathways. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH3. The function of MADH3 has been established by previous studies. Zhang et al. (1996) showed that MADH3 and MADH4 (SMAD4; 600993) synergized to induce strong ligand-independent TGF-beta-like responses. MADH3 containing a C-terminal truncation acted as a dominant-negative inhibitor of the normal TGF-beta response. The activity of MADH3 was regulated by the TGF-beta receptors (e.g., 190181), and MADH3 was phosphorylated and associated with the ligand-bound receptor complex. Zhang et al. (1996) stated that these results define MADH3 as an effector of the TGF-beta response. Zawel et al. (1998) found that human SMAD3 and SMAD4 proteins could specifically recognize an identical 8-bp palindromic sequence (GTCTAGAC). Tandem repeats of this palindrome conferred striking TGF-beta responsiveness to a minimal promoter. This responsiveness was abrogated by targeted deletion of the cellular SMAD4 gene. These results showed that SMAD proteins are involved in the biologic Animal

model experiments lend further support to the function of MADH3. Zhu et al. (1998) reported the targeted disruption of the mouse Smad3 gene. Smad3 mutant mice were viable and fertile. Between 4 and 6 months of age, the Smad3 mutant mice became moribund with colorectal adenocarcinomas. The neoplasms penetrated through the intestinal wall and metastasized to lymph nodes. Since TGF-beta transduces its signal to the interior of the cell via Smad2, Smad3, and Smad4, these results directly implicate TGF-beta signaling in the pathogenesis of colorectal cancer and provide a compelling animal model for the study of human colorectal cancer

[11884] It is appreciated that the abovementioned animal model for MADH3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11885] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11886] Zawel, L.; Dai, J. L.; Buckhaults, P.; Zhou, S.; Kinzler, K. W.; Vogelstein, B.; Kern, S. E. : Human Smad3 and Smad4 are sequence-specific transcription activators. Molec. Cell 1: 611-617, 1998. ; and

[11887] Zhu, Y.; Richardson, J. A.; Parada, L. F.; Graff, J. M. :
Smad3 mutant mice develop metastatic colorectal cancer.
Cell 94: 703–714, 1998.

[11888] Further studies establishing the function and utilities of
MADH3 are found in John Hopkins OMIM database record
ID 603109, and in cited publications numbered 8579,
12349, 6480, 7824, 783 and 8580–8581 listed in the
bibliography section hereinbelow, which are also hereby
incorporated by reference. Microtubule-associated Protein,
RP/EB Family, Member 2 (MAPRE2, Accession NM_014268)
is another VGAM178 host target gene. MAPRE2 BINDING
SITE is HOST TARGET binding site found in the 3` un-
translated region of mRNA encoded by MAPRE2, corre-
sponding to a HOST TARGET binding site such as BINDING
SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-
trates the complementarity of the nucleotide sequences of
MAPRE2 BINDING SITE, designated SEQ ID:15545, to the
nucleotide sequence of VGAM178 RNA, herein designated
VGAM RNA, also designated SEQ ID:2889.

[11889] Another function of VGAM178 is therefore inhibition of
Microtubule-associated Protein, RP/EB Family, Member 2
(MAPRE2, Accession NM_014268), a gene which The func-
tional inactivation of the APC gene product is a key event

in colorectal tumorigenesis. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE2. The function of MAPRE2 has been established by previous studies. EB1 family proteins (e.g., MAPRE1; 603108) interact with cytoplasmic microtubules in interphase cells, with mitotic spindles, and with the adenomatous polyposis coli (APC; 175100) tumor suppressor gene. The functional inactivation of the APC gene product is a key event in colorectal tumorigenesis. By differential mRNA display of resting and activated T cells, followed by 5-prime RACE, Renner et al. (1997) isolated a cDNA encoding MAPRE2, which they termed RP1. The deduced 327-amino acid protein has significant homology with EB1 family proteins. Northern blot analysis detected a 2.6-kb transcript in T cells activated by 2 signals (i.e., cell surface antigen(s) and/or cytokine) and also in lymphocyte tumor cell lines. Immunoprecipitation analysis indicated that RP1 associates with full-length but not C terminus-deleted APC. Renner et al. (1997) concluded that RP1 may be an immediate-early T-cell regulatory gene. Using immunoprecipitation analysis, Juwana et al. (1999) showed that the N terminus of RP1 interacted with monomeric or polymer-

ized tubulin in fibrosarcoma cell lines. Immunofluorescence microscopy demonstrated that RP1 is localized in the plus ends of microtubule networks in the presence or absence of APC. By radiation hybrid and sequence analyses, Su and Qi (2001) mapped the MAPRE2 gene to 18q12. By FISH, Wadle et al. (2001) assigned the gene to 18q21.

[11890] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11891] Juwana, J.-P.; Henderikx, P.; Mischo, A.; Wadle, A.; Fadle, N.; Gerlach, K.; Arends, J. W.; Hoogenboom, H.; Pfreundschuh, M.; Renner, C. : EB/RP gene family encodes tubulin binding proteins. *Int. J. Cancer* 81: 275–284, 1999. ; and

[11892] Renner, C.; Pfitzenmeier, J.-P.; Gerlach, K.; Held, G.; Ohnesorge, S.; Sahin, U.; Bauer, S.; Pfreundschuh, M. : RP1, a new member of the adenomatous polyposis coli-binding EB1-like gen.

[11893] Further studies establishing the function and utilities of MAPRE2 are found in John Hopkins OMIM database record ID 605789, and in cited publications numbered 734–73 and 8578 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Microtubule-associated Protein Tau (MAPT, Acces-

sion NM_005910) is another VGAM178 host target gene. MAPT BINDING SITE1 through MAPT BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAPT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPT BINDING SITE1 through MAPT BINDING SITE4, designated SEQ ID:12538, SEQ ID:18826, SEQ ID:18832 and SEQ ID:18838 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11894] Another function of VGAM178 is therefore inhibition of Microtubule-associated Protein Tau (MAPT, Accession NM_005910), a gene which Microtubule-associated protein tau; promotes microtubule assembly. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPT. The function of MAPT has been established by previous studies. The microtubule-associated proteins (MAPs) coassemble with tubulin (see OMIM Ref. No. 602529) into microtubules in vitro. Microtubule-associated protein tau appears to be enriched in axons. Neve et

al. (1986) identified tau cDNA clones in a human fetal brain cDNA library. The clones recognized a 6-kb message that was expressed in human brain but not in other human tissues and exhibited a developmental shift in size. By screening cDNA libraries prepared from the frontal cortex of an Alzheimer disease patient and from fetal human brain, Goedert et al. (1988) isolated the cDNA for a core protein of the paired helical filament of Alzheimer disease (OMIM Ref. No. 104300). The partial amino acid sequence of this core protein was used to design synthetic oligonucleotide probes. The cDNA encodes a protein of 352 amino acids that contains a characteristic amino acid repeat in its carboxyl-terminal half. Because of extensive homology to the sequence of the mouse microtubule-associated protein tau, they stated that this protein must constitute the human equivalent of mouse tau. Tau protein mRNA was found in normal amounts in the frontal cortex from patients with Alzheimer disease. Hutton et al. (1998) studied 13 families in which an autosomal dominant inherited dementia, frontotemporal dementia with parkinsonism (OMIM Ref. No. 600274), had been shown to be linked to chromosome 17. The authors stated that this disorder has historically been termed Pick dis-

ease (OMIM Ref. No. 172700). Most cases showed neuronal and/or glial inclusions that stained positively with antibodies raised against tau, although the tau pathology varied considerably in both its quantity (or severity) and characteristics. This form of dementia, symbolized FTDP17 by them, had been mapped to a 2-cM region on 17q21.11. Since the tau gene was known to lie within this region and because the disorder was recognized to be a 'tauopathy,' Hutton et al. (1998) sequenced the MAPT gene in the thirteen 17-linked families and identified 3 missense mutations (gly272 to val, 157140.0002; pro301 to leu, 157140.0001; and arg406 to trp, 157140.0003) and 3 mutations in the 5-prime splice site of exon 10. All of the splice site mutations destabilized a potential stem-loop structure that is probably involved in regulating the alternative splicing of exon 10 (Goedert et al., 1989). This caused more frequent usage of the 5-prime splice site and an increased proportion of tau transcripts that include exon 10. The increase in exon 10+ mRNA was expected to increase the proportion of tau containing 4 microtubule-binding repeats, which is consistent with the neuropathology described in families with FTDP17. Hong et al. (1998) indicated that more than 10 exonic and intronic

mutations of the MAPT gene had been identified in about 20 FTDP17 families. They found that analyses of soluble and insoluble tau proteins from brains of FTDP17 patients indicated that different pathogenic mutations differentially altered distinct biochemical properties and stoichiometry of brain tau isoforms. Functional assays of recombinant tau proteins with different FTDP17 missense mutations implicated all but 1 of these mutations in disease pathogenesis by reducing the ability of tau to bind microtubules and promote microtubule assembly. In a study of frontotemporal dementia in the Netherlands during the period January 1994 to June 1998, Rizzu et al. (1999) found 37 patients who had one or more first-degree relatives with dementia. A mutation in the MAPT gene was found in 17.8% of the group of patients with FTDP17 and in 43% of patients with FTDP17 who also had a positive family history of the disorder. Three distinct missense mutations, G272V (157140.0002), P301L (157140.0001), and R406W (157140.0003), accounted for 15.6% of the mutations. These 3 missense mutations, and a single amino acid deletion, K280del, that was detected in 1 patient, strongly reduced the ability of tau to promote microtubule assembly. In some FTDP17 families, MAPT mutations have not

been found, suggesting locus and/or allelic heterogeneity. Rizzu et al. (1999) suggested that the MAPT mutations may result in disturbances in the interactions of the protein tau with microtubules, resulting in hyperphosphorylation of tau protein, assembly into filaments, and subsequent cell death. Verpillat et al. (2002) found that the tau H1/H1 genotype was significantly overrepresented in 100 patients with frontotemporal dementia compared to controls (odds ratio for H1/H1 = 1.95). In addition, there was a significant negative effect in carriers of both the H1/H1 genotype and the APOE2 allele (OMIM Ref. No. 107741). The association of intronic mutations in the MAPT gene in frontotemporal dementia with parkinsonism (e.g., 157140.0004) highlights the involvement of aberrant pre-mRNA splicing in the pathogenesis of neurodegenerative disorders. To establish a model system for studying the role of pre-mRNA splicing in neurodegenerative diseases, Jiang et al. (2000) constructed a MAPT minigene that reproduced alternative splicing in both cultured cells and in vitro biochemical assays. They demonstrated that mutations in a nonconserved intronic region of the human MAPT gene led to increased splicing between exons 10 and 11. Systematic biochemical analyses indicated the im-

portance of U1 snRNP (OMIM Ref. No. 180740) and, to a lesser extent, U6 snRNP (OMIM Ref. No. 180692) in differentially recognizing wildtype versus intron-mutant MAPT pre-mRNAs. Goedert et al. (1998) reviewed the role of tau mutations in frontotemporal dementias. Heutink (2000) reviewed the role of tau protein in frontotemporal dementia and other neurodegenerative disorders. Hutton (2001) reviewed the known missense and splice site mutations in the tau gene that are associated with disease and described different mechanisms involved in pathogenesis, including disruption of the interaction between tau and tubulin, deposition of abnormal tau filaments, and the generation of abnormal ratios of tau isoforms. Animal model experiments lend further support to the function of MAPT. Lewis et al. (2000) demonstrated that expression of human tau containing the most common mutation, P301L (157140.0001), results in motor and behavioral deficits in transgenic mice, with age- and gene-dose-dependent development of neurofibrillary tangles (NFT).

[11895] It is appreciated that the abovementioned animal model for MAPT is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11896] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11897] Hutton, M.; Lendon, C. L.; Rizzu, P.; Baker, M.; Froelich, S.; Houlden, H.; Pickering-Brown, S.; Chakraverty, S.; Isaacs, A.; Grover, A.; Hackett, J.; Adamson, J.; and 39 others : Association of missense and 5-prime-splice-site mutations in tau with the inherited dementia FTDP-17. *Nature* 393: 702-705, 1998. ; and

[11898] Rizzu, P.; Van Swieten, J. C.; Joosse, M.; Hasegawa, M.; Stevens, M.; Tibben, A.; Niermeijer, M. F.; Hillebrand, M.; Ravid, R.; Oostra, B. A.; Goedert, M.; van Duijn, C. M.; Heutink, P.

[11899] Further studies establishing the function and utilities of MAPT are found in John Hopkins OMIM database record ID 157140, and in cited publications numbered 11119-11133, 1212, 11134-11142, 11160, 11165-11164, 413 and 11166-1683 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Membrane Protein, Palmitoylated 3 (MAGUK p55 subfamily member 3) (MPP3, Accession NM_001932) is another VGAM178 host target gene. MPP3 BINDING SITE is HOST TARGET binding site found in the

5` untranslated region of mRNA encoded by MPP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP3 BINDING SITE, designated SEQ ID:7641, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11900] Another function of VGAM178 is therefore inhibition of Membrane Protein, Palmitoylated 3 (MAGUK p55 subfamily member 3) (MPP3, Accession NM_001932). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP3. Musashi Homolog 1 (Drosophila) (MSI1, Accession NM_002442) is another VGAM178 host target gene. MSI1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MSI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSI1 BINDING SITE, designated SEQ ID:8283, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11901] Another function of VGAM178 is therefore inhibition of

Musashi Homolog 1 (Drosophila) (MSI1, Accession NM_002442). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSI1. Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM_002474) is another VGAM178 host target gene. MYH11 BINDING SITE1 and MYH11 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MYH11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYH11 BINDING SITE1 and MYH11 BINDING SITE2, designated SEQ ID:8301 and SEQ ID:23143 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11902] Another function of VGAM178 is therefore inhibition of Myosin, Heavy Polypeptide 11, Smooth Muscle (MYH11, Accession NM_002474), a gene which is involved in muscle contraction. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYH11. The function of MYH11 has been established by previous studies. Mat-

suoka et al. (1991, 1993) isolated a smooth muscle myosin heavy-chain gene from a human cDNA library. They confirmed it as a smooth muscle MHC gene by Northern blot hybridization and a partial DNA sequence analysis. By study of human/Chinese hamster and human/mouse hybrid cells and by in situ hybridization, they localized the gene to 16q12.1. This localization was later found to be an error and the gene was shown, in fact, to be located on the short arm of chromosome 16 in a region involved in pericentric inversion inv(16)(OMIM Ref. No. p13q22), a characteristic abnormality associated with acute myeloid leukemia, most commonly of the M4Eo subtype. Liu et al. (1993) pinpointed the 16p and 16q breakpoints by yeast artificial chromosome and cosmid cloning and identified the 2 genes involved in the inversion. On 16p, the MYH11 gene was interrupted; on 16q, the inversion occurred near the end of the coding region for CBF-beta (OMIM Ref. No. 121360), also known as PEBP2-beta, a subunit of a heterodimeric transcription factor regulating genes expressed in T cells. In all of 6 inv(16) patients tested, an in-frame fusion messenger RNA was demonstrated that connected the first 165 amino acids of CBFB with the tail region of MYH11. The repeated

coiled coil of MYH11 may result in dimerization of the CBFB fusion protein, which in turn would lead to alterations in transcriptional regulation and contribute to leukemic transformation. Deng et al. (1993) mapped the MYH11 gene to the middle of the short arm of chromosome 16 by fluorescence in situ hybridization. Southern blots of a panel of hybrids containing different portions of human chromosome 16 localized the gene to 16p13.13–p13.12. Studies of DNA from a CHO/mouse hybrid clone mapping panel showed that the gene was located on mouse chromosome 16. Castilla et al. (1999) showed that the fusion Cbfb–MYH11 blocks myeloid differentiation in mice and predisposes the mice to acute myelomonocytic leukemia when exposed to N-ethyl–N-nitrosourea (ENU), a potent DNA alkylating mutagen.

[11903] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11904] Castilla, L. H.; Garrett, L.; Adya, N.; Orlic, D.; Dutra, A.; Anderson, S.; Owens, J.; Eckhaus, M.; Bodine, D.; Liu, P. P. : The fusion gene Cbfb–MYH11 blocks myeloid differentiation and predisposes mice to acute myelomonocytic

leukaemia. (Letter) Nature Genet. 23: 144–146, 1999. ;
and

[11905] Liu, P.; Tarle, S. A.; Hajra, A.; Claxton, D. F.; Marlton, P.;
Freedman, M.; Siciliano, M. J.; Collins, F. S. : Fusion be-
tween transcription factor CBF-beta/PEBP2-beta and a
myosin heav.

[11906] Further studies establishing the function and utilities of
MYH11 are found in John Hopkins OMIM database record
ID 160745, and in cited publications numbered
3222–3223, 3403, 460 and 4607 listed in the bibliogra-
phy section hereinbelow, which are also hereby incorpo-
rated by reference. Neurexin 2 (NRXN2, Accession
NM_138732) is another VGAM178 host target gene.
NRXN2 BINDING SITE1 through NRXN2 BINDING SITE3 are
HOST TARGET binding sites found in untranslated regions
of mRNA encoded by NRXN2, corresponding to HOST
TARGET binding sites such as BINDING SITE I, BINDING
SITE II or BINDING SITE III. Table 2 illustrates the comple-
mentarity of the nucleotide sequences of NRXN2 BINDING
SITE1 through NRXN2 BINDING SITE3, designated SEQ
ID:28981, SEQ ID:28987 and SEQ ID:17465 respectively,
to the nucleotide sequence of VGAM178 RNA, herein des-
ignated VGAM RNA, also designated SEQ ID:2889.

[11907] Another function of VGAM178 is therefore inhibition of Neurexin 2 (NRXN2, Accession NM_138732), a gene which may be involved in cell recognition, cell adhesion, and may mediate intracellular signaling. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN2. The function of NRXN2 has been established by previous studies. Neurexins are polymorphic cell surface proteins that are expressed in neurons. Neurexin II is 1 of 3 rat neurexin genes identified by Ushkaryov et al. (1992). Each gene contains 2 promoters that direct synthesis of alpha- and beta-neurexins. By analysis of a 1.2-Mb region flanking the MEN1 (OMIM Ref. No. 131100) locus on 11q13, Bergman et al. (1999) identified MCG36, a human gene similar to rat neurexin II-alpha. By genomic sequence analysis, Tabuchi and Sudhof (2002) determined that the NRXN2 gene contains 23 exons, has very large introns, and spans 106 kb, making it a relatively small gene compared to NRXN1 (OMIM Ref. No. 600565) and NRXN3. Exon 1 is more than 2 kb and encodes the first LNS domain and the first EGF-like repeat of alpha-neurexins. Other exons are average in size, with the remaining LNS domains interrupted by at least 1 intron, whereas all EGF-

like repeats are encoded in single exons. The last exon, also relatively large, encodes the transmembrane region and cytoplasmic tail. Tabuchi and Sudhof (2002) also described a number of neurexin splice sites.

[11908] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11909] Bergman, L.; Silins, G.; Grimmond, S.; Hummerich, H.; Stewart, C.; Little, P.; Hayward, N. : A 500-kb sequence-ready cosmid contig and transcript map of the MEN1 region on 11q13. *Genomics* 55: 49–56, 1999. ; and

[11910] Tabuchi, K.; Sudhof, T. C. : Structure and evolution of neurexin genes: insight into the mechanism of alternative splicing. *Genomics* 79: 849–859, 2002.

[11911] Further studies establishing the function and utilities of NRXN2 are found in John Hopkins OMIM database record ID 600566, and in cited publications numbered 9529, 9525–952 and 9530 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAD23 Homolog B (*S. cerevisiae*) (RAD23B, Accession NM_002874) is another VGAM178 host target gene.

RAD23B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

RAD23B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD23B BINDING SITE, designated SEQ ID:8784, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11912] Another function of VGAM178 is therefore inhibition of RAD23 Homolog B (*S. cerevisiae*) (RAD23B, Accession NM_002874), a gene which is involved in dna excision repair. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD23B. The function of RAD23B has been established by previous studies. Volker et al. (2001) described the assembly of the nucleotide excision repair (NER) complex in normal and repair-deficient (xeroderma pigmentosum) human cells by employing a novel technique of local ultraviolet irradiation combined with fluorescent antibody labeling. The damage-recognition complex XPC-HHR23B (OMIM Ref. No. RAD23B) appeared to be essential for the recruitment of all subsequent NER factors in the preincision complex, including transcription repair factor TFIIH (see OMIM Ref.

No. 189972). The authors found that XPA (OMIM Ref. No. 278700) associates relatively late, is required for anchoring of ERCC1 (OMIM Ref. No. 126380)–XPF (OMIM Ref. No. 133520), and may be essential for activation of the endonuclease activity of XPG (OMIM Ref. No. 133530). These findings identified XPC as the earliest known NER factor in the reaction mechanism, gave insight into the order of subsequent NER components, provided evidence for a dual role of XPA, and supported a concept of sequential assembly of repair proteins at the site of damage rather than a preassembled repairosome. Animal model experiments lend further support to the function of RAD23B. Ng et al. (2002) created a Rad23B knockout mouse model. Fibroblasts cultured from embryonic animals were not UV sensitive and retained the repair characteristics of wild-type cells, suggesting that Rad23A can functionally replace Rad23B in NER. However, there was a high rate of intrauterine or neonatal death in Rad23B $-/-$ animals, and surviving animals displayed a variety of abnormalities, including retarded growth, facial dysmorphology, and male sterility. These findings suggested a function for Rad23B in normal development that cannot be compensated for by Rad23A.

- [11913] It is appreciated that the abovementioned animal model for RAD23B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.
- [11914] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [11915] Volker, M.; Mone, M. J.; Karmakar, P.; van Hoffen, A.; Schul, W.; Vermeulen, W.; Hoeijmakers, J. H. J.; van Driel, R.; van Zeeland, A. A.; Mullenders, L. H. F. : Sequential assembly of the nucleotide excision repair factors in vivo. *Molec. Cell* 8: 213–224, 2001. ; and
- [11916] Ng, J. M. Y.; Vrieling, H.; Sugasawa, K.; Ooms, M. P.; Grootegeod, J. A.; Vreeburg, J. T. M.; Visser, P.; Beems, R. B.; Gorgels, T. G. M. F.; Hanaoka, F.; Hoeijmakers, J. H. J.; van der.
- [11917] Further studies establishing the function and utilities of RAD23B are found in John Hopkins OMIM database record ID 600062, and in sited publications numbered 8410, 8793–879 and 8249 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732) is another VGAM178 host target gene.

RAD50 BINDING SITE1 and RAD50 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by RAD50, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD50 BINDING SITE1 and RAD50 BINDING SITE2, designated SEQ ID:12293 and SEQ ID:28550 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11918] Another function of VGAM178 is therefore inhibition of RAD50 Homolog (*S. cerevisiae*) (RAD50, Accession NM_005732), a gene which is involved in dna double-strand break repair (dsbr). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD50. The function of RAD50 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132.RAR-related Orphan Receptor B (RORB, Accession NM_006914) is another VGAM178 host target gene. RORB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

RORB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RORB BINDING SITE, designated SEQ ID:13785, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11919] Another function of VGAM178 is therefore inhibition of RAR-related Orphan Receptor B (RORB, Accession NM_006914), a gene which is an orphan nuclear receptor. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RORB. The function of RORB has been established by previous studies. ROR-beta is a transcription factor and belongs to the nuclear receptor family (Carlberg et al., 1994). Members of this superfamily share a common modular structure composed of a transactivation domain, a DNA-binding domain, and a ligand-binding domain (Evans, 1988). Typically, their transcriptional transactivation function is regulated by small lipophilic molecules, such as steroid hormones, vitamin D, retinoic acids, and thyroid hormone. These molecules are synthesized in the organism and pass readily through the plasma membrane to reach the corresponding receptors

inside the cell. In addition to the classic hormone receptors, a growing number of nuclear receptors for which no ligands are known have been identified by homology cloning. These nuclear receptors are referred to as 'orphan' nuclear receptors. ROR-beta is such an orphan nuclear receptor, forming a subfamily with the closely related nuclear receptors ROR-alpha (RORA; 600825) and ROR-gamma (RORC; 602943). Animal model experiments lend further support to the function of RORB. ROR-beta is expressed in areas of the central nervous system that are involved in the processing of sensory information, including spinal cord, thalamus, and sensory cerebellar cortices. Additionally, ROR-beta localizes to the 3 principal anatomic components of the mammalian timing system: the suprachiasmatic nuclei, the retina, and the pineal gland. Andre et al. (1998) showed that RORB mRNA levels oscillate in retina and pineal gland with a circadian rhythm that persists in constant darkness. They generated RORB-deficient mice by gene targeting in embryonic stem cells and analyzed their phenotypic behavior. Rorb $-/-$ mice display a duck-like gait, transient male incapability to reproduce sexually, and a severely disorganized retina that suffers from postnatal degeneration. Consequently, adult

Rorb $-/-$ mice are blind, yet their circadian activity rhythm is still entrained by light-dark cycles. Under conditions of constant darkness, Rorb $-/-$ mice display an extended period of free-running rhythmicity. The overall behavioral phenotype of Rorb $-/-$ mice, together with the chromosomal localization of the gene on mouse chromosome 4, suggested a close relationship to the spontaneous mouse mutation 'vacillans' described by Sirlin (1956) and now thought to be extinct

[11920] It is appreciated that the abovementioned animal model for RORB is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[11921] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11922] Evans, R. M. : The steroid and thyroid hormone receptor superfamily. Science 240: 889–895, 1988. ; and

[11923] Andre, E.; Conquet, F.; Steinmayr, M.; Stratton, S. C.; Porciatti, V.; Becker-Andre, M. : Disruption of retinoid-related orphan receptor beta changes circadian behavior, causes retinal deg.

[11924] Further studies establishing the function and utilities of

RORB are found in John Hopkins OMIM database record ID 601972, and in cited publications numbered 8522, 8523–852 and 7778 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Smoothed Homolog (Drosophila) (SMOH, Accession NM_005631) is another VGAM178 host target gene. SMOH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMOH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMOH BINDING SITE, designated SEQ ID:12161, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11925] Another function of VGAM178 is therefore inhibition of Smoothed Homolog (Drosophila) (SMOH, Accession NM_005631). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMOH. Suppression of Tumorigenicity 7 (ST7, Accession NM_021908) is another VGAM178 host target gene. ST7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by ST7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7 BINDING SITE, designated SEQ ID:22428, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11926] Another function of VGAM178 is therefore inhibition of Suppression of Tumorigenicity 7 (ST7, Accession NM_021908), a gene which has a role in regulating cell-environment or cell-cell interactions. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7. The function of ST7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM178 host target gene. SYNGR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNGR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SYNGR1 BINDING SITE, designated SEQ ID:11061, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11927] Another function of VGAM178 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481) is another VGAM178 host target gene. TCF2 BINDING SITE1 and TCF2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF2 BINDING SITE1 and TCF2 BINDING SITE2, designated SEQ ID:13199 and SEQ

ID:6073 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11928] Another function of VGAM178 is therefore inhibition of Transcription Factor 2, Hepatic; LF-B3; Variant Hepatic Nuclear Factor (TCF2, Accession NM_006481), a gene which probably binds to the inverted palindrome 5'-gttaatnattaac-3'. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF2. The function of TCF2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM118.Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660) is another VGAM178 host target gene. TGFB1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TGFB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB1 BINDING SITE, designated SEQ ID:6318, to the nucleotide sequence of VGAM178 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2889.

[11929] Another function of VGAM178 is therefore inhibition of Transforming Growth Factor, Beta 1 (Camurati-Engelmann disease) (TGFB1, Accession NM_000660). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB1. Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM_049695) is another VGAM178 host target gene. VANGL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VANGL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VANGL2 BINDING SITE, designated SEQ ID:35475, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11930] Another function of VGAM178 is therefore inhibition of Vang-like 2 (van gogh, Drosophila) (VANGL2, Accession XM_049695), a gene which may take part in defining the lateral boundary of floorplate differentiation. Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with VANGL2. The function of VANGL2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM111. Wingless-type MMTV Integration Site Family Member 2 (WNT2, Accession NM_003391) is another VGAM178 host target gene. WNT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT2 BINDING SITE, designated SEQ ID:9427, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11931] Another function of VGAM178 is therefore inhibition of Wingless-type MMTV Integration Site Family Member 2 (WNT2, Accession NM_003391), a gene which is the ligand for members of the frizzled family of seven transmembrane receptors. probable developmental protein and may be a signaling molecule . Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT2. The function of WNT2 has been established by previous

studies. Wainwright et al. (1988) cloned from a human lung cDNA library an expressed gene sequence that was identified by isolation of a methylation-free CpG island from human chromosome 7. (Bird et al. (1985) described so-called HTF (HpaII tiny fragments) islands which are relatively rich in G/C and virtually free of methylation at the CpG dinucleotide. Such regions usually occur at discrete units, 1 to 2 kb long, which can be detected by analysis with methylation-sensitive restriction enzymes. HTF islands are particularly associated with the site of initiation of transcription and the first exons of genes. Both tissue-specific and housekeeping genes have been described in association with HTF islands (Bird, 1987). The characteristics of HTF islands make it possible to isolate selectively regions of the genome that are likely to contain structural genes.) As part of the strategy to isolate the gene for cystic fibrosis (OMIM Ref. No. 219700), Wainwright et al. (1988) found and characterized a coding sequence with marked similarity to the murine protooncogene *Int1* and its *Drosophila* homolog 'wingless,' but which was distinct from the human *INT1* gene located on chromosome 12 (OMIM Ref. No. 164820). Indirect evidence that *INT1* is secreted and that the product of 'wingless' is a diffusible

gene product suggests that these proteins are secreted growth factors. Wainwright et al. (1988) suggested that the INT1-related protein is an additional member of the INT1 growth factor gene family. Because of its homology to protooncogene INT1, IRP is also symbolized INT1L1. IRP is expressed in a variety of fetal and adult human tissues that do not overlap with the pattern of expression of INT1. Chan et al. (1989) isolated overlapping genomic clones that correspond to the mouse homolog of the IRP gene and demonstrated in mouse-hamster somatic cell hybrids that the gene is located on mouse chromosome 6. In addition, they showed that the mouse *Int1l1* and *Met* genes coamplified in lines of spontaneously transformed mouse NIH 3T3 cells, indicating that these genes are closely linked. IRP is about 500 kb from MET (OMIM Ref. No. 164860); the CFTR gene (OMIM Ref. No. 602421) is in the 500-kb interval between IRP and a point 1,000 kb from MET. Anonymous probe J3.11 is about 500 kb farther distally. Nusse et al. (1991) suggested that IRP be referred to as WNT2. Wassink et al. (2001) examined WNT2 as a candidate gene for autism (OMIM Ref. No. 209850) for the following reasons: first, the WNT family of genes influences the development of numerous organs and systems,

including the central nervous system; second, WNT2 is located in the 7q31–q33 region linked to autism and is adjacent to a chromosomal breakpoint in an individual with autism; third, a mouse knockout of the dishevelled–1 (DVL1; 601365) gene, a member of a gene family essential for the function of the WNT pathway, exhibits a behavioral phenotype characterized primarily by diminished social interaction. Wassink et al. (2001) found 2 families containing nonconservative coding sequence variants that segregated with autism. They also identified linkage disequilibrium between a WNT2 3–prime–untranslated region single nucleotide polymorphism (SNP) and their sample of autism–affected sib pair families and trios (2 parents and 1 affected child). Linkage disequilibrium occurred almost exclusively in a subgroup of affected sib pair families defined by the presence of severe language abnormalities and was also found to be associated with evidence for linkage to 7q. Expression analysis demonstrated WNT2 expression in the human thalamus. Using ribonuclease protection analysis, Huguet et al. (1994) investigated expression of WNT genes, including WNT2, in human cell lines, as well as in normal, benign, and malignant breast tissue. They detected WNT2 in human breast tissue and

hypothesized that WNT2 may be associated with abnormal proliferation in breast tissue. In a later study, McCoy et al. (2002) could find no significant association between autistic disorder and WNT2 genotypes in either an overall dataset or a language-impaired subset of families. No activating mutation in the coding region of WNT2 was found.

[11932] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[11933] Wainwright, B. J.; Scambler, P. J.; Stanier, P.; Watson, E. K.; Bell, G.; Wicking, C.; Estivill, X.; Courtney, M.; Bour, A.; Pedersen, P. S.; Williamson, R.; Farrall, M. : Isolation of a human gene with protein sequence similarity to human and murine int-1 and the Drosophila segment polarity mutant wingless. EMBO J. 7: 1743–1748, 1988. ; and

[11934] Wassink, T. H.; Piven, J.; Vieland, V. J.; Huang, J.; Swiderski, R. E.; Pietila, J.; Braun, T.; Beck, G.; Folstein, S. E.; Haines, J. L.; Sheffield, V. C. : Evidence supporting WNT2 as a.

[11935] Further studies establishing the function and utilities of WNT2 are found in John Hopkins OMIM database record ID 147870, and in cited publications numbered 3469, 392

and 3968–3973 listed in the bibliography section herein–below, which are also hereby incorporated by reference. BIKE (Accession NM_017593) is another VGAM178 host target gene. BIKE BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BIKE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIKE BINDING SITE, designated SEQ ID:19038, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11936] Another function of VGAM178 is therefore inhibition of BIKE (Accession NM_017593). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIKE. Baculoviral IAP Repeat–containing 4 (BIRC4, Accession NM_001167) is another VGAM178 host target gene. BIRC4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BIRC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

BIRC4 BINDING SITE, designated SEQ ID:6834, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11937] Another function of VGAM178 is therefore inhibition of Baculoviral IAP Repeat-containing 4 (BIRC4, Accession NM_001167). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC4. Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152) is another VGAM178 host target gene. C20orf12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf12 BINDING SITE, designated SEQ ID:19957, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11938] Another function of VGAM178 is therefore inhibition of Chromosome 20 Open Reading Frame 12 (C20orf12, Accession NM_018152). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with C20orf12. Calpain 6 (CAPN6, Accession NM_014289) is another VGAM178 host target gene. CAPN6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN6 BINDING SITE, designated SEQ ID:15566, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11939] Another function of VGAM178 is therefore inhibition of Calpain 6 (CAPN6, Accession NM_014289). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN6. Deiodinase, Iodothyronine, Type II (DIO2, Accession NM_013989) is another VGAM178 host target gene. DIO2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DIO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIO2 BINDING SITE, designated SEQ ID:15175,

to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11940] Another function of VGAM178 is therefore inhibition of Deiodinase, Iodothyronine, Type II (DIO2, Accession NM_013989). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIO2. DKFZP434H132 (Accession XM_057020) is another VGAM178 host target gene. DKFZP434H132 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434H132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H132 BINDING SITE, designated SEQ ID:36444, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11941] Another function of VGAM178 is therefore inhibition of DKFZP434H132 (Accession XM_057020). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H132. DKFZP434L0718 (Accession NM_032139) is another VGAM178 host target gene. DK-

FZP434L0718 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434L0718, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L0718 BINDING SITE, designated SEQ ID:25819, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11942] Another function of VGAM178 is therefore inhibition of DKFZP434L0718 (Accession NM_032139). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L0718. DKFZp547O146 (Accession NM_020224) is another VGAM178 host target gene. DKFZp547O146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547O146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547O146 BINDING SITE, designated SEQ ID:21486, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2889.

[11943] Another function of VGAM178 is therefore inhibition of DKFZp547O146 (Accession NM_020224). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547O146. Ephrin-A5 (EFNA5, Accession NM_001962) is another VGAM178 host target gene. EFNA5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EFNA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EFNA5 BINDING SITE, designated SEQ ID:7684, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11944] Another function of VGAM178 is therefore inhibition of Ephrin-A5 (EFNA5, Accession NM_001962). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EFNA5. FLJ00001 (Accession XM_088525) is another VGAM178 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39774, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11945] Another function of VGAM178 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ12076 (Accession NM_025187) is another VGAM178 host target gene. FLJ12076 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12076, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12076 BINDING SITE, designated SEQ ID:24823, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11946] Another function of VGAM178 is therefore inhibition of FLJ12076 (Accession NM_025187). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ12076. FLJ12363 (Accession NM_032167) is another VGAM178 host target gene. FLJ12363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12363 BINDING SITE, designated SEQ ID:25865, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11947] Another function of VGAM178 is therefore inhibition of FLJ12363 (Accession NM_032167). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12363. FLJ13441 (Accession NM_023924) is another VGAM178 host target gene. FLJ13441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13441 BINDING SITE, designated SEQ ID:23391, to the nucleotide sequence of

VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11948] Another function of VGAM178 is therefore inhibition of FLJ13441 (Accession NM_023924). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13441. FLJ14594 (Accession NM_032808) is another VGAM178 host target gene. FLJ14594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14594, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14594 BINDING SITE, designated SEQ ID:26565, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11949] Another function of VGAM178 is therefore inhibition of FLJ14594 (Accession NM_032808). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14594. FLJ20898 (Accession NM_024600) is another VGAM178 host target gene. FLJ20898 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ20898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20898 BINDING SITE, designated SEQ ID:23850, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11950] Another function of VGAM178 is therefore inhibition of FLJ20898 (Accession NM_024600). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20898. FLJ21603 (Accession NM_024762) is another VGAM178 host target gene. FLJ21603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21603 BINDING SITE, designated SEQ ID:24118, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11951] Another function of VGAM178 is therefore inhibition of FLJ21603 (Accession NM_024762). Accordingly, utilities of

VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21603. FLJ22938 (Accession NM_024676) is another VGAM178 host target gene. FLJ22938 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22938, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22938 BINDING SITE, designated SEQ ID:23985, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11952] Another function of VGAM178 is therefore inhibition of FLJ22938 (Accession NM_024676). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22938. GW112 (Accession NM_006418) is another VGAM178 host target gene. GW112 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GW112, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GW112 BINDING SITE, designated

SEQ ID:13130, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11953] Another function of VGAM178 is therefore inhibition of GW112 (Accession NM_006418). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GW112. Histamine Receptor H3 (HRH3, Accession NM_007232) is another VGAM178 host target gene. HRH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HRH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HRH3 BINDING SITE, designated SEQ ID:14107, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11954] Another function of VGAM178 is therefore inhibition of Histamine Receptor H3 (HRH3, Accession NM_007232). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HRH3. KIAA0446 (Accession XM_044155) is another VGAM178 host target gene. KIAA0446 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34146, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11955] Another function of VGAM178 is therefore inhibition of KIAA0446 (Accession XM_044155). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0446. KIAA0563 (Accession NM_014834) is another VGAM178 host target gene. KIAA0563 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0563 BINDING SITE, designated SEQ ID:16840, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11956] Another function of VGAM178 is therefore inhibition of

KIAA0563 (Accession NM_014834). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0563. KIAA0630 (Accession XM_114729) is another VGAM178 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43059, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11957] Another function of VGAM178 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. KIAA0773 (Accession NM_014690) is another VGAM178 host target gene. KIAA0773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0773 BINDING SITE, designated SEQ ID:16193, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11958] Another function of VGAM178 is therefore inhibition of KIAA0773 (Accession NM_014690). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0773. KIAA0903 (Accession XM_049251) is another VGAM178 host target gene. KIAA0903 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0903 BINDING SITE, designated SEQ ID:35371, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11959] Another function of VGAM178 is therefore inhibition of KIAA0903 (Accession XM_049251). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0903. KIAA1016 (Accession XM_166260) is another

VGAM178 host target gene. KIAA1016 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1016 BINDING SITE, designated SEQ ID:44084, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11960] Another function of VGAM178 is therefore inhibition of KIAA1016 (Accession XM_166260). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1016. KIAA1554 (Accession XM_170834) is another VGAM178 host target gene. KIAA1554 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1554, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1554 BINDING SITE, designated SEQ ID:45609, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11961] Another function of VGAM178 is therefore inhibition of KIAA1554 (Accession XM_170834). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1554. KIAA1582 (Accession XM_037262) is another VGAM178 host target gene. KIAA1582 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1582, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1582 BINDING SITE, designated SEQ ID:32584, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11962] Another function of VGAM178 is therefore inhibition of KIAA1582 (Accession XM_037262). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1582. KIAA1817 (Accession XM_042978) is another VGAM178 host target gene. KIAA1817 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1817, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1817 BINDING SITE, designated SEQ ID:33861, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11963] Another function of VGAM178 is therefore inhibition of KIAA1817 (Accession XM_042978). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1817. KIAA1853 (Accession XM_045184) is another VGAM178 host target gene. KIAA1853 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1853 BINDING SITE, designated SEQ ID:34383, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11964] Another function of VGAM178 is therefore inhibition of KIAA1853 (Accession XM_045184). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1853. KIAA1940 (Accession XM_086981) is another VGAM178 host target gene. KIAA1940 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1940 BINDING SITE, designated SEQ ID:39004, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11965] Another function of VGAM178 is therefore inhibition of KIAA1940 (Accession XM_086981). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1940. Myristoylated Alanine-rich Protein Kinase C Substrate (MARCKS, Accession NM_002356) is another VGAM178 host target gene. MARCKS BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MARCKS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MARCKS BINDING SITE, designated SEQ ID:8166, to the nucleotide

sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11966] Another function of VGAM178 is therefore inhibition of Myristoylated Alanine-rich Protein Kinase C Substrate (MARCKS, Accession NM_002356). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MARCKS. MGC15619 (Accession NM_032369) is another VGAM178 host target gene. MGC15619 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15619, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15619 BINDING SITE, designated SEQ ID:26158, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11967] Another function of VGAM178 is therefore inhibition of MGC15619 (Accession NM_032369). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15619. MGC20460 (Accession NM_053043) is another VGAM178 host target gene. MGC20460 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC20460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20460 BINDING SITE, designated SEQ ID:27586, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11968] Another function of VGAM178 is therefore inhibition of MGC20460 (Accession NM_053043). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20460. MGC2744 (Accession XM_017557) is another VGAM178 host target gene. MGC2744 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC2744, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2744 BINDING SITE, designated SEQ ID:30325, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11969] Another function of VGAM178 is therefore inhibition of

MGC2744 (Accession XM_017557). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2744. MGC3248 (Accession NM_032486) is another VGAM178 host target gene. MGC3248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3248 BINDING SITE, designated SEQ ID:26237, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11970] Another function of VGAM178 is therefore inhibition of MGC3248 (Accession NM_032486). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3248. NIR3 (Accession XM_038799) is another VGAM178 host target gene. NIR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NIR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of NIR3 BINDING SITE, designated SEQ ID:32926, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11971] Another function of VGAM178 is therefore inhibition of NIR3 (Accession XM_038799). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NIR3. Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635) is another VGAM178 host target gene. P2RX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P2RX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P2RX1 BINDING SITE, designated SEQ ID:33352, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11972] Another function of VGAM178 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with P2RX1. Paternally Expressed 10 (PEG10, Accession NM_015068) is another VGAM178 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ ID:17424, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11973] Another function of VGAM178 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM_015068). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792) is another VGAM178 host target gene. PTPNS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PTPNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of PTPNS1 BINDING SITE, designated SEQ ID:28050, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11974] Another function of VGAM178 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type Substrate 1 (PTPNS1, Accession NM_080792). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPNS1. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942) is another VGAM178 host target gene. RPS6KA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA4 BINDING SITE, designated SEQ ID:10052, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11975] Another function of VGAM178 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942). Accordingly, utilities of

VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA4. SCAMP-4 (Accession NM_079834) is another VGAM178 host target gene. SCAMP-4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAMP-4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAMP-4 BINDING SITE, designated SEQ ID:27819, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11976] Another function of VGAM178 is therefore inhibition of SCAMP-4 (Accession NM_079834). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAMP-4. SCLY (Accession NM_016510) is another VGAM178 host target gene. SCLY BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCLY, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCLY BINDING SITE, designated SEQ

ID:18589, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11977] Another function of VGAM178 is therefore inhibition of SCLY (Accession NM_016510). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCLY. Septin 3 (SEPT3, Accession NM_019106) is another VGAM178 host target gene. SEPT3 BINDING SITE1 and SEPT3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SEPT3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT3 BINDING SITE1 and SEPT3 BINDING SITE2, designated SEQ ID:21178 and SEQ ID:21177 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11978] Another function of VGAM178 is therefore inhibition of Septin 3 (SEPT3, Accession NM_019106). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with SEPT3. Solute Carrier Family 12 (potassium/chloride transporters), Member 8 (SLC12A8, Accession NM_024628) is another VGAM178 host target gene. SLC12A8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC12A8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A8 BINDING SITE, designated SEQ ID:23893, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11979] Another function of VGAM178 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 8 (SLC12A8, Accession NM_024628). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A8. SFRS Protein Kinase 1 (SRPK1, Accession NM_003137) is another VGAM178 host target gene. SRPK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SRPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SRPK1 BINDING SITE, designated SEQ ID:9109, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11980] Another function of VGAM178 is therefore inhibition of SFRS Protein Kinase 1 (SRPK1, Accession NM_003137). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRPK1. Uronyl-2-sulfotransferase (UST, Accession NM_005715) is another VGAM178 host target gene. UST BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UST BINDING SITE, designated SEQ ID:12270, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11981] Another function of VGAM178 is therefore inhibition of Uronyl-2-sulfotransferase (UST, Accession NM_005715). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with UST. VELI1 (Accession NM_004664) is another VGAM178 host target gene. VELI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VELI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VELI1 BINDING SITE, designated SEQ ID:11037, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11982] Another function of VGAM178 is therefore inhibition of VELI1 (Accession NM_004664). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VELI1. LOC126823 (Accession XM_059086) is another VGAM178 host target gene. LOC126823 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC126823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126823 BINDING SITE, designated SEQ ID:36863, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA,

also designated SEQ ID:2889.

[11983] Another function of VGAM178 is therefore inhibition of LOC126823 (Accession XM_059086). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126823. LOC129303 (Accession XM_059343) is another VGAM178 host target gene. LOC129303 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC129303, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129303 BINDING SITE, designated SEQ ID:36969, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11984] Another function of VGAM178 is therefore inhibition of LOC129303 (Accession XM_059343). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129303. LOC146108 (Accession XM_085322) is another VGAM178 host target gene. LOC146108 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146108, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146108 BINDING SITE, designated SEQ ID:38061, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11985] Another function of VGAM178 is therefore inhibition of LOC146108 (Accession XM_085322). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146108. LOC146237 (Accession XM_096954) is another VGAM178 host target gene. LOC146237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146237 BINDING SITE, designated SEQ ID:40665, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11986] Another function of VGAM178 is therefore inhibition of LOC146237 (Accession XM_096954). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC146237. LOC146745 (Accession XM_085577) is another VGAM178 host target gene. LOC146745 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146745, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146745 BINDING SITE, designated SEQ ID:38231, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11987] Another function of VGAM178 is therefore inhibition of LOC146745 (Accession XM_085577). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146745. LOC147071 (Accession XM_054031) is another VGAM178 host target gene. LOC147071 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147071 BINDING SITE, designated SEQ ID:36134, to

the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11988] Another function of VGAM178 is therefore inhibition of LOC147071 (Accession XM_054031). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147071. LOC147669 (Accession XM_097262) is another VGAM178 host target gene. LOC147669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147669 BINDING SITE, designated SEQ ID:40853, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11989] Another function of VGAM178 is therefore inhibition of LOC147669 (Accession XM_097262). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147669. LOC148255 (Accession XM_086120) is another VGAM178 host target gene. LOC148255 BINDING SITE1 and LOC148255 BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by LOC148255, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148255 BINDING SITE1 and LOC148255 BINDING SITE2, designated SEQ ID:38498 and SEQ ID:38499 respectively, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11990] Another function of VGAM178 is therefore inhibition of LOC148255 (Accession XM_086120). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148255. LOC148946 (Accession XM_097557) is another VGAM178 host target gene. LOC148946 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148946 BINDING SITE, designated SEQ ID:40936, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11991] Another function of VGAM178 is therefore inhibition of LOC148946 (Accession XM_097557). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148946. LOC149296 (Accession XM_086481) is another VGAM178 host target gene. LOC149296 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149296 BINDING SITE, designated SEQ ID:38693, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11992] Another function of VGAM178 is therefore inhibition of LOC149296 (Accession XM_086481). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149296. LOC151174 (Accession XM_098013) is another VGAM178 host target gene. LOC151174 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151174, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151174 BINDING SITE, designated SEQ ID:41310, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11993] Another function of VGAM178 is therefore inhibition of LOC151174 (Accession XM_098013). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151174. LOC162333 (Accession XM_102591) is another VGAM178 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42126, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11994] Another function of VGAM178 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC162333. LOC163412 (Accession XM_088868) is another VGAM178 host target gene. LOC163412 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163412, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163412 BINDING SITE, designated SEQ ID:39951, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11995] Another function of VGAM178 is therefore inhibition of LOC163412 (Accession XM_088868). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163412. LOC196027 (Accession XM_113633) is another VGAM178 host target gene. LOC196027 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196027, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196027 BINDING SITE, designated SEQ ID:42304, to the nucleotide sequence of VGAM178 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2889.

[11996] Another function of VGAM178 is therefore inhibition of LOC196027 (Accession XM_113633). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196027. LOC196955 (Accession XM_085210) is another VGAM178 host target gene. LOC196955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196955 BINDING SITE, designated SEQ ID:37926, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11997] Another function of VGAM178 is therefore inhibition of LOC196955 (Accession XM_085210). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196955. LOC197408 (Accession XM_117031) is another VGAM178 host target gene. LOC197408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197408, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197408 BINDING SITE, designated SEQ ID:43206, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11998] Another function of VGAM178 is therefore inhibition of LOC197408 (Accession XM_117031). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197408. LOC200251 (Accession XM_114173) is another VGAM178 host target gene. LOC200251 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200251 BINDING SITE, designated SEQ ID:42754, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[11999] Another function of VGAM178 is therefore inhibition of LOC200251 (Accession XM_114173). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC200251. LOC201173 (Accession XM_113312) is another VGAM178 host target gene. LOC201173 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201173 BINDING SITE, designated SEQ ID:42213, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12000] Another function of VGAM178 is therefore inhibition of LOC201173 (Accession XM_113312). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201173. LOC201220 (Accession XM_113321) is another VGAM178 host target gene. LOC201220 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201220, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201220 BINDING SITE, designated SEQ ID:42220, to

the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12001] Another function of VGAM178 is therefore inhibition of LOC201220 (Accession XM_113321). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201220. LOC201243 (Accession XM_113935) is another VGAM178 host target gene. LOC201243 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201243, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201243 BINDING SITE, designated SEQ ID:42553, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12002] Another function of VGAM178 is therefore inhibition of LOC201243 (Accession XM_113935). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201243. LOC220739 (Accession XM_167548) is another VGAM178 host target gene. LOC220739 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220739, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220739 BINDING SITE, designated SEQ ID:44655, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12003] Another function of VGAM178 is therefore inhibition of LOC220739 (Accession XM_167548). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220739. LOC253715 (Accession XM_173053) is another VGAM178 host target gene. LOC253715 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253715 BINDING SITE, designated SEQ ID:46310, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12004] Another function of VGAM178 is therefore inhibition of LOC253715 (Accession XM_173053). Accordingly, utilities

of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253715. LOC255565 (Accession XM_170811) is another VGAM178 host target gene. LOC255565 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC255565, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255565 BINDING SITE, designated SEQ ID:45590, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12005] Another function of VGAM178 is therefore inhibition of LOC255565 (Accession XM_170811). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255565. LOC256273 (Accession XM_172847) is another VGAM178 host target gene. LOC256273 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC256273, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256273 BINDING SITE, designated SEQ ID:46124, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12006] Another function of VGAM178 is therefore inhibition of LOC256273 (Accession XM_172847). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256273. LOC90525 (Accession XM_032304) is another VGAM178 host target gene. LOC90525 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90525 BINDING SITE, designated SEQ ID:31638, to the nucleotide sequence of VGAM178 RNA, herein designated VGAM RNA, also designated SEQ ID:2889.

[12007] Another function of VGAM178 is therefore inhibition of LOC90525 (Accession XM_032304). Accordingly, utilities of VGAM178 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90525. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 179 (VGAM179) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12008] VGAM179 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM179 was detected is described hereinabove with reference to Figs. 1–8.

[12009] VGAM179 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12010] VGAM179 gene encodes a VGAM179 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM179 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM179 precursor RNA is designated SEQ ID:165, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:165 is located at position 69393 relative to the genome of

Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12011] VGAM179 precursor RNA folds onto itself, forming VGAM179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12012] An enzyme complex designated DICER COMPLEX, `dices` the VGAM179 folded precursor RNA into VGAM179 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM179 RNA is designated SEQ ID:2890, and is provided hereinbelow with reference to the sequence listing part.

[12013] VGAM179 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM179 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[12014] VGAM179 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM179 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM179 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM179 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[12015] The complementary binding of VGAM179 RNA, herein designated VGAM RNA, to host target binding sites on VGAM179 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM179 host target RNA into VGAM179 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12016] It is appreciated that VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM179 host target genes. The mRNA of each one of this plurality of VGAM179 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM179 RNA, herein designated VGAM RNA, and which when bound by VGAM179 RNA causes inhibition of translation of respective one or more VGAM179

host target proteins.

[12017] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM179 gene, herein designated VGAM GENE, on one or more VGAM179 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12018] It is yet further appreciated that a function of VGAM179 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syn-

drome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM179 correlate with, and may be deduced from, the identity of the host target genes which VGAM179 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12019] Nucleotide sequences of the VGAM179 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM179 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM179 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM179 are further described hereinbelow with reference to Table 1.

[12020] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM179 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM179 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12021] As mentioned hereinabove with reference to Fig. 1, a function of VGAM179 gene, herein designated VGAM is inhibition of expression of VGAM179 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM179 correlate with, and may be deduced from, the identity of the target genes which VGAM179 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12022] Acid Phosphatase 1, Soluble (ACP1, Accession NM_004300) is a VGAM179 host target gene. ACP1 BINDING SITE1 and ACP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP1 BINDING SITE1 and ACP1 BINDING SITE2, designated SEQ ID:10509 and SEQ ID:13959 respectively, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12023] A function of VGAM179 is therefore inhibition of Acid Phosphatase 1, Soluble (ACP1, Accession NM_004300), a gene which as demonstrated in starch-gel electrophoresis. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP1. The function of ACP1 has

been established by previous studies. Hopkinson et al. (1963) described a new human polymorphism involving erythrocyte acid phosphatase (EC 3.1.3.2) as demonstrated in starch-gel electrophoresis. Three alleles, P(a), P(b) and P(c), are thought to be involved, their frequency being estimated to be 0.35, 0.60 and 0.05, respectively. Another rare allele, P(r), was described by Giblett and Scott (1965). Mohrenweiser and Novotny (1982) described a low activity variant of ACP1 that is frequent (gene frequency of 0.132) in Guaymi Indians of Central America. Data on gene frequencies of allelic variants were tabulated by Roychoudhury and Nei (1988). Red cells of persons with the GUA-1 phenotype had increased basal levels of the flavoenzyme glutathione reductase and a larger fraction of the glutathione reductase protein in the form of the holoenzyme, indicating increased levels of flavin adenine dinucleotide in the red cells of these persons. The finding was consistent with the suggestion that ACP1 has a physiologic function as a flavin mononucleotide phosphatase. This function could regulate the intracellular concentrations of flavin coenzymes and, ultimately, of flavoenzymes, and could be the mechanism for the association between ACP1 type and certain disease states.

Sensabaugh and Golden (1978) showed that ACP1 is inhibited by folic acid and various folates, and that the inhibition is phenotype dependent: ACP1(C) more than ACP1(A) more than ACP1(B). This explains elevation of ACP levels in red cells of patients with megaloblastic anemia and also variation in incidence and severity of favism in G6PD-deficient persons. Swallow et al. (1973) showed that 'red cell' acid phosphatase is not limited to erythrocytes but can be demonstrated in other tissues, including cultured fibroblasts and lymphoblastoid cells where there is no possibility of contamination by blood. Dissing et al. (1991) concluded that 2 electrophoretically distinct isozymes, f and s, which are produced in allele-specific ratios and are associated with each of the 3 major alleles, are generated by alternative splicing of the primary RNA transcript. 2. Junien et al. (1979) assigned the ACP1 locus to 2p25. Larson et al. (1982) studied 4 patients who had inherited an unbalanced form of a familial reciprocal translocation, $t(2;10)(p24;q26)$, giving them partial duplication of 2p. Increased levels of acid phosphatase indicated that ACP1 is located in the 2p24–2pter region and that MDH is not. The previous inconsistency of the SRO (smallest region of overlap) is now resolved; ACP1 is at

2p25. Wo et al. (1992) cloned genes encoding 2 low molecular weight phosphotyrosyl protein phosphatases from a human placenta cDNA library. They were found to have identical nucleotide sequences, with the exception of a 108-bp segment in the middle of the open reading frame. From further studies they concluded that the 2 represent the fast and slow electrophoretic forms of red cell acid phosphatase and that this enzyme is not unique to the red cell but instead is expressed in all human tissues. They examined a human chromosome 2-specific library and demonstrated that the sequences they were studying are located on chromosome 2.

[12024] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12025] Dissing, J.; Johnsen, A. H.; Sensabaugh, G. F. : Human red cell acid phosphatase (ACP1): the amino acid sequence of the two isozymes Bf and Bs encoded by the ACP1*B allele. J. Biol. Chem. 266: 20619–20625, 1991. ; and

[12026] Wo, Y.-Y. P.; McCormack, A. L.; Shabanowitz, J.; Hunt, D. F.; Davis, J. P.; Mitchell, G. L.; Van Etten, R. L. : Sequencing, cloning, and expression of human red cell-type acid phosphata.

[12027] Further studies establishing the function and utilities of ACP1 are found in John Hopkins OMIM database record ID 171500, and in cited publications numbered 11035–11039, 11204, 11234, 11236–11242, 11206, 11243–11248, 3478, 11249–11259, 3780, 1126 and 11261–1853 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Adrenergic, Beta–3–, Receptor (ADRB3, Accession NM_000025) is another VGAM179 host target gene. ADRB3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ADRB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADRB3 BINDING SITE, designated SEQ ID:5459, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12028] Another function of VGAM179 is therefore inhibition of Adrenergic, Beta–3–, Receptor (ADRB3, Accession NM_000025), a gene which stimulates adenylyl cyclase activity and regulates lipolysis. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with ADRB3. The function of ADRB3 has been established by previous studies. Emorine et al. (1989) isolated a third beta-adrenergic receptor, beta-3-adrenergic receptor (ADRB3). (See ADRB1 (OMIM Ref. No. 109630) and ADRB2 (OMIM Ref. No. 109690).) Exposure of eukaryotic cells transfected with this gene to adrenaline or noradrenaline promoted the accumulation of adenosine 3-prime,5-prime-monophosphate. The potency of beta-AR agonists and inhibitors was described. Van Spronsen et al. (1993) demonstrated that the transcription-start sites of the mouse and human ADRB3 mRNA are located in a region comprised between 150 and 200 nucleotides 5-prime from the ATG translation-start codon. Motifs potentially implicated in heterologous regulation of ADRB3 expression by glucocorticoids and by beta-adrenergic agonists were identified upstream from these cap sites. Van Spronsen et al. (1993) also described the exon/intron structure of the genes. Their results suggested that utilization of alternate promoters and/or 3-prime untranslated regions may allow tissue-specific regulation of the expression of ADRB3. Wilkie et al. (1993) presented a list of G protein-coupled receptor genes (their Table 3), indi-

cating that the ADRB3 gene had been mapped to 8p12–p11.2 and the homologous gene to mouse chromosome 8. Animal model experiments lend further support to the function of ADRB3. Bachman et al. (2002) created mice that lacked the beta–adrenergic receptors ADRB1, ADRB2, and ADRB3. Beta–less mice on a chow diet had a reduced metabolic rate and were slightly obese. On a high–fat diet, beta–less mice, in contrast to wildtype mice, developed massive obesity that was due entirely to a failure of diet–induced thermogenesis.

[12029] It is appreciated that the abovementioned animal model for ADRB3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12030] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12031] Van Spronsen, A.; Nahmias, C.; Krief, S.; Briend–Sutren, M.–M.; Strosberg, A. D.; Emorine, L. J. : The promoter and intron/exon structure of the human and mouse beta–3–adrenergic–receptor genes. *Europ. J. Biochem.* 213: 1117–1124, 1993. ; and

[12032] Bachman, E. S.; Dhillon, H.; Zhang, C.–Y.; Cinti, S.; Bianco,

A. C.; Kobilka, B. K.; Lowell, B. B. : Beta-AR signaling required for diet-induced thermogenesis and obesity resistance. Sci.

[12033] Further studies establishing the function and utilities of ADRB3 are found in John Hopkins OMIM database record ID 109691, and in cited publications numbered 1446, 4273-4274, 3172, 4275-4284, 4286, 4287-428 and 11892 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Ca++ Transporting, Cardiac Muscle, Slow Twitch 2 (ATP2A2, Accession NM_001681) is another VGAM179 host target gene. ATP2A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP2A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP2A2 BINDING SITE, designated SEQ ID:7401, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12034] Another function of VGAM179 is therefore inhibition of ATPase, Ca++ Transporting, Cardiac Muscle, Slow Twitch 2 (ATP2A2, Accession NM_001681). Accordingly, utilities

of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP2A2. Betaine-homocysteine Methyltransferase 2 (BHMT2, Accession NM_017614) is another VGAM179 host target gene. BHMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHMT2 BINDING SITE, designated SEQ ID:19116, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12035] Another function of VGAM179 is therefore inhibition of Betaine-homocysteine Methyltransferase 2 (BHMT2, Accession NM_017614). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHMT2. Breast Cancer 1, Early Onset (BRCA1, Accession NM_007294) is another VGAM179 host target gene. BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BRCA1, corresponding to HOST TARGET binding sites such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRCA1 BINDING SITE1 through BRCA1 BINDING SITE10, designated SEQ ID:14162, SEQ ID:14168, SEQ ID:14174, SEQ ID:14180, SEQ ID:14187, SEQ ID:14193, SEQ ID:14199, SEQ ID:14207, SEQ ID:14213 and SEQ ID:14219 respectively, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12036] Another function of VGAM179 is therefore inhibition of Breast Cancer 1, Early Onset (BRCA1, Accession NM_007294). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRCA1. UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminy)-galactosylglucosylceramide N-acetylgalactosaminyltransferase (GalNAc-T) (GALGT, Accession NM_001478) is another VGAM179 host target gene. GALGT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

GALGT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALGT BINDING SITE, designated SEQ ID:7209, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12037] Another function of VGAM179 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminyl)-galactosylglucosylceramide N-acetylgalactosaminyltransferase (GalNAc-T) (GALGT, Accession NM_001478), a gene which is involved in the biosynthesis of gangliosides gm2, gd2 and ga2. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALGT. The function of GALGT has been established by previous studies. The G(M2) and G(D2) gangliosides are sialic acid-containing glycosphingolipids involved in signal transduction and cell-cell recognition.

Nagata et al. (1992) used expression cloning to isolate the cDNA encoding the enzyme responsible for generating G(M2) and G(D2) glycosphingolipids. This gene is termed beta-1,4-N-acetylgalactosaminyltransferase (GalNAc-T) (EC 2.4.1.92), or G(M2)/G(D2) synthase. The cDNA encodes a 561-amino acid polypeptide. Northern blot analysis revealed that the gene is expressed as 2 differently sized transcripts in all cells tested that expressed G(MS), G(D2), or both. These findings indicate that the cDNAs catalyze the transfer of GalNAc into G(M3) and G(D3) by a beta-1,4 linkage, resulting in the synthesis of G(M2) and G(D2), respectively. Animal model experiments lend further support to the function of GALGT. Niemann-Pick disease type C (NPC; 267220) is a progressive neurodegenerative disorder caused by mutations in the NPC1 gene and characterized by intracellular accumulation of cholesterol and sphingolipids. To determine the relative contribution of ganglioside accumulation in the neuropathogenesis of Niemann-Pick C disease, Liu et al. (2000) bred NPC model mice with mice carrying a targeted mutation in GalNAc-T. Unlike the NPC model mice, the double mutant mice did not exhibit central nervous system (CNS) accumulation of gangliosides GM2 or of glycolipids GA1 and

GA2. Histologic analysis revealed that the characteristic neuronal storage pathology of NPC disease was substantially reduced in the double mutant mice. By contrast, visceral pathology was similar in the NPC and double mutant mice. Most notably, the clinical phenotype of the double mutant mice, in the absence of CNS ganglioside accumulation and associated neuronal pathology, did not improve. The authors concluded that complex ganglioside storage, while responsible for much of the neuronal pathology, did not significantly influence the clinical phenotype of the NPC model.

[12038] It is appreciated that the abovementioned animal model for GALGT is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12039] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12040] Liu, Y.; Wu, Y.-P.; Wada, R.; Neufeld, E. B.; Mullin, K. A.; Howard, A. C.; Pentchev, P. G.; Vanier, M. T.; Suzuki, K.; Proia, R. L. : Alleviation of neuronal ganglioside storage does not improve the clinical course of the Niemann–Pick C disease mouse. *Hum. Molec. Genet.* 9: 1087–1092,

2000. ; and

[12041] Nagata, Y.; Yamashiro, S.; Yodoi, J.; Lloyd, K. O.; Shiku, H.; Furukawa, K. : Expression cloning of beta-1,4-N-acetylgalactosaminyltransferase cDNAs that determine the expression of G.

[12042] Further studies establishing the function and utilities of GALGT are found in John Hopkins OMIM database record ID 601873, and in cited publications numbered 1291, 129 and 11383 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hepatic Leukemia Factor (HLF, Accession NM_002126) is another VGAM179 host target gene. HLF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLF BINDING SITE, designated SEQ ID:7902, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12043] Another function of VGAM179 is therefore inhibition of Hepatic Leukemia Factor (HLF, Accession NM_002126). Accordingly, utilities of VGAM179 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with HLF. Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430) is another VGAM179 host target gene. MN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MN1 BINDING SITE, designated SEQ ID:8272, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12044] Another function of VGAM179 is therefore inhibition of Meningioma (disrupted in balanced translocation) 1 (MN1, Accession NM_002430). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MN1. Retinoic Acid Receptor, Beta (RARβ, Accession NM_016152) is another VGAM179 host target gene. RARβ BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by RARβ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of RARB BINDING SITE, designated SEQ ID:18238, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12045] Another function of VGAM179 is therefore inhibition of Retinoic Acid Receptor, Beta (RARB, Accession NM_016152), a gene which is one member of the steroid/thyroid hormone receptor family of ligand-activated transcription factors. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RARB. The function of RARB has been established by previous studies. The 3 retinoic acid receptors, alpha (RARA; 180240), beta (RARB), and gamma (RARG; 180190), are members of the nuclear receptor superfamily. Retinoic acid was the first morphogen described in vertebrates. The RARA and RARB genes are more homologous to those of the 2 closely related thyroid hormone receptors THRA and THRB, located on chromosomes 17 and 3, respectively, than to any other members of the nuclear receptor family. These observations suggest that the thyroid hormone and retinoic acid receptors evolved by gene, and possibly chromosome, duplications from a common ancestor which itself di-

verged rather early in evolution from the common ancestor of the steroid receptor group of the family. The RARB gene, formerly symbolized HAP, maps to 3p24 by somatic cell hybridization and in situ hybridization. Benbrook et al. (1988) showed a predominant distribution in epithelial tissues and therefore used the designation RAR(epsilon). By in situ hybridization, Mattei et al. (1988) assigned the RARB gene to 3p24. Using deletion mapping, de The et al. (1990) identified a 27-bp fragment located 59-bp upstream of the transcriptional start, which confers retinoic acid responsiveness on the herpesvirus thymidine kinase promoter. They found indications that both alpha and beta receptors act through the same DNA sequence. Mattei et al. (1991) assigned the corresponding gene to chromosome 14, band A, in the mouse, and to chromosome 15 in the rat. Nadeau et al. (1992) confirmed assignment of the mouse homolog to the centromeric portion of chromosome 14. From a comparison of a hepatitis-B virus (HBV) integration site present in a particular human hepatocellular carcinoma (HCC; 114550) with the corresponding unoccupied site in the nontumorous tissue of the same liver, Dejean et al. (1986) found that HBV integration placed the viral sequence next to a liver cell sequence that

bears a striking resemblance to both an oncogene, ERBA (OMIM Ref. No. 190120), and the supposed DNA-binding domain of the human glucocorticoid receptor (OMIM Ref. No. 138040) and estrogen receptor (OMIM Ref. No. 133430) genes. Dejean et al. (1986) suggested that this gene, usually silent or transcribed at a very low level in normal hepatocytes, becomes inappropriately expressed as a consequence of HBV integration, thus contributing to the cell transformation. By means of a panel of rodent-human somatic cell hybrid DNAs, Dejean et al. (1986) localized the gene to chromosome 3. Further studies by de The et al. (1987) suggested that the HAP gene product may be a novel ligand-responsive regulatory protein whose inappropriate expression in liver is related to hepatocellular carcinogenesis. Brand et al. (1988) showed that the novel protein called HAP (for HBV-activated protein) is a retinoic acid receptor. They referred to this receptor as the beta type (RARβ) and mapped it to 3p25-p21.

[12046] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12047] Benbrook, D.; Lernhardt, E.; Pfahl, M. : A new retinoic acid receptor identified from a hepatocellular carcinoma.

(Letter) Nature 333: 669–672, 1988. ; and

[12048] de The, H.; Marchio, A.; Tiollais, P.; Dejean, A. : A novel steroid thyroid hormone receptor–related gene inappropriately expressed in human hepatocellular carcinoma. Nature 330: 667–670.

[12049] Further studies establishing the function and utilities of RARB are found in John Hopkins OMIM database record ID 180220, and in cited publications numbered 5669–5672, 5709, 5728–573 and 11147–5732 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Reelin (RELN, Accession XM_168628) is another VGAM179 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45281, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12050] Another function of VGAM179 is therefore inhibition of Reelin (RELN, Accession XM_168628), a gene which regulates microtubule function in neurons and neuronal mi–

gration. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35.Spinocerebellar Ataxia 7 (olivopontocerebellar atrophy with retinal degeneration) (SCA7, Accession NM_000333) is another VGAM179 host target gene. SCA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCA7 BINDING SITE, designated SEQ ID:5883, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12051] Another function of VGAM179 is therefore inhibition of Spinocerebellar Ataxia 7 (olivopontocerebellar atrophy with retinal degeneration) (SCA7, Accession NM_000333). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCA7. SH3-domain Binding Protein 4

(SH3BP4, Accession NM_014521) is another VGAM179 host target gene. SH3BP4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SH3BP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SH3BP4 BINDING SITE, designated SEQ ID:15852, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12052] Another function of VGAM179 is therefore inhibition of SH3-domain Binding Protein 4 (SH3BP4, Accession NM_014521), a gene which is of unknown function, contains SH3-domain binding protein 4; similar to the EH-binding protein. Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SH3BP4. The function of SH3BP4 has been established by previous studies. A major element of the cornea is a transparent stroma produced and maintained by corneal fibroblasts, or keratocytes. Using differential display of RNA from normal and macular corneal dystrophy cultured keratocytes, followed by screening a corneal fibroblast library, Dunlevy et al.

(1999) identified a cDNA encoding SH3BP4. The deduced 963-amino acid SH3BP4 protein contains 3 asn-pro-phe (NPF) motifs, which are EPS15 (OMIM Ref. No. 600051) homology (EH)-binding sites (see OMIM Ref. No. NUBP1; 603728); an SH3 domain; a PXXP motif; a bipartite nuclear targeting signal; and a tyrosine phosphorylation site. Sequence analysis predicted that SH3BP4 is identical to a 479-amino acid EH-binding protein (Wong et al., 1995) except for the presence of an additional 73 N-terminal and 411 mid- to C-terminal residues in SH3BP4. Northern blot analysis revealed ubiquitous expression of a 5.6-kb transcript, with highest levels in pancreas, low levels in kidney, skeletal muscle, and liver, and lowest levels in lung and brain. Expression was also detected in cultured normal keratocytes. Using FISH, Dunlevy et al. (1999) mapped the SH3BP4 gene to 2q37.1-q37.2.

[12053] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12054] Dunlevy, J. R.; Berryhill, B. L.; Vergnes, J.-P.; SundarRaj, N.; Hassell, J. R. : Cloning, chromosomal localization, and characterization of cDNA from a novel gene, SH3BP4, expressed by human corneal fibroblasts. Genomics 62:

519–524, 1999. ; and

[12055] Wong, W. T.; Schumacher, C.; Salcini, A. E.; Romano, A.; Castagnino, P.; Pelicci, P. G.; DiFiore, P. P. : A protein-binding domain, EH, identified in the receptor tyrosine kinase substrat.

[12056] Further studies establishing the function and utilities of SH3BP4 are found in John Hopkins OMIM database record ID 605611, and in cited publications numbered 6768–6769 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transmembrane Protein 1 (TMEM1, Accession NM_003274) is another VGAM179 host target gene. TMEM1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TMEM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEM1 BINDING SITE, designated SEQ ID:9290, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12057] Another function of VGAM179 is therefore inhibition of Transmembrane Protein 1 (TMEM1, Accession

NM_003274). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEM1. BNIP-S (Accession NM_138278) is another VGAM179 host target gene. BNIP-S BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BNIP-S, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BNIP-S BINDING SITE, designated SEQ ID:28689, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12058] Another function of VGAM179 is therefore inhibition of BNIP-S (Accession NM_138278). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BNIP-S. C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM_031910) is another VGAM179 host target gene. C1QTNF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QTNF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of C1QTNF6 BINDING SITE, designated SEQ ID:25655, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12059] Another function of VGAM179 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 6 (C1QTNF6, Accession NM_031910). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF6. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728) is another VGAM179 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38836, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12060] Another function of VGAM179 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728). Accordingly, utilities of VGAM179

include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. Choline Kinase (CHK, Accession NM_001277) is another VGAM179 host target gene. CHK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHK BINDING SITE, designated SEQ ID:6944, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12061] Another function of VGAM179 is therefore inhibition of Choline Kinase (CHK, Accession NM_001277). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHK. Cbp/p300-interacting Transactivator, with Glu/Asp-rich Carboxy-terminal Domain, 2 (CITED2, Accession NM_006079) is another VGAM179 host target gene. CITED2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CITED2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of CITED2 BINDING SITE, designated SEQ ID:12726, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12062] Another function of VGAM179 is therefore inhibition of Cbp/p300–interacting Transactivator, with Glu/Asp–rich Carboxy–terminal Domain, 2 (CITED2, Accession NM_006079). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CITED2. CTP Synthase II (CTPS2, Accession NM_019857) is another VGAM179 host target gene. CTPS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CTPS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTPS2 BINDING SITE, designated SEQ ID:21261, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12063] Another function of VGAM179 is therefore inhibition of CTP Synthase II (CTPS2, Accession NM_019857). Accord–

ingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTPS2. FLJ13782 (Accession NM_024915) is another VGAM179 host target gene. FLJ13782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13782 BINDING SITE, designated SEQ ID:24436, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12064] Another function of VGAM179 is therefore inhibition of FLJ13782 (Accession NM_024915). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13782. JIK (Accession NM_016281) is another VGAM179 host target gene. JIK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JIK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JIK BINDING SITE, designated SEQ ID:18405, to

the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12065] Another function of VGAM179 is therefore inhibition of JIK (Accession NM_016281). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JIK. Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM_004979) is another VGAM179 host target gene. KCND1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCND1 BINDING SITE, designated SEQ ID:11422, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12066] Another function of VGAM179 is therefore inhibition of Potassium Voltage-gated Channel, Shal-related Subfamily, Member 1 (KCND1, Accession NM_004979). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCND1. KIAA0240 (Accession XM_166479) is another

VGAM179 host target gene. KIAA0240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0240 BINDING SITE, designated SEQ ID:44406, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12067] Another function of VGAM179 is therefore inhibition of KIAA0240 (Accession XM_166479). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0240. KIAA0417 (Accession XM_048898) is another VGAM179 host target gene. KIAA0417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0417 BINDING SITE, designated SEQ ID:35288, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12068] Another function of VGAM179 is therefore inhibition of KIAA0417 (Accession XM_048898). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0417. KIAA1509 (Accession XM_029353) is another VGAM179 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30875, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12069] Another function of VGAM179 is therefore inhibition of KIAA1509 (Accession XM_029353). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. MGC1127 (Accession NM_033549) is another VGAM179 host target gene. MGC1127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC1127, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1127 BINDING SITE, designated SEQ ID:27308, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12070] Another function of VGAM179 is therefore inhibition of MGC1127 (Accession NM_033549). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1127. SP192 (Accession NM_021639) is another VGAM179 host target gene. SP192 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SP192, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP192 BINDING SITE, designated SEQ ID:22295, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12071] Another function of VGAM179 is therefore inhibition of SP192 (Accession NM_021639). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP192.

Testis-specific Kinase 2 (TESK2, Accession XM_032399) is another VGAM179 host target gene. TESK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK2 BINDING SITE, designated SEQ ID:31651, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12072] Another function of VGAM179 is therefore inhibition of Testis-specific Kinase 2 (TESK2, Accession XM_032399). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TESK2. LOC122830 (Accession XM_058661) is another VGAM179 host target gene. LOC122830 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC122830, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122830 BINDING SITE, designated SEQ ID:36705, to the nucleotide sequence of

VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12073] Another function of VGAM179 is therefore inhibition of LOC122830 (Accession XM_058661). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC122830. LOC220846 (Accession XM_165515) is another VGAM179 host target gene. LOC220846 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220846 BINDING SITE, designated SEQ ID:43661, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12074] Another function of VGAM179 is therefore inhibition of LOC220846 (Accession XM_165515). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220846. LOC55580 (Accession NM_017571) is another VGAM179 host target gene. LOC55580 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC55580, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55580 BINDING SITE, designated SEQ ID:18995, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12075] Another function of VGAM179 is therefore inhibition of LOC55580 (Accession NM_017571). Accordingly, utilities of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55580. LOC91948 (Accession XM_041723) is another VGAM179 host target gene. LOC91948 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91948, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91948 BINDING SITE, designated SEQ ID:33573, to the nucleotide sequence of VGAM179 RNA, herein designated VGAM RNA, also designated SEQ ID:2890.

[12076] Another function of VGAM179 is therefore inhibition of LOC91948 (Accession XM_041723). Accordingly, utilities

of VGAM179 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91948. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 180 (VGAM180) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12077] VGAM180 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM180 was detected is described hereinabove with reference to Figs. 1–8.

[12078] VGAM180 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12079] VGAM180 gene encodes a VGAM180 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM180 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM180 precursor RNA is designated SEQ ID:166, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:166 is located at position 10036 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12080] VGAM180 precursor RNA folds onto itself, forming VGAM180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12081] An enzyme complex designated DICER COMPLEX, `dices` the VGAM180 folded precursor RNA into VGAM180 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide se-

quence of VGAM180 RNA is designated SEQ ID:2891, and is provided hereinbelow with reference to the sequence listing part.

[12082] VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM180 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[12083] VGAM180 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM180 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM180 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[12084] The complementary binding of VGAM180 RNA, herein designated VGAM RNA, to host target binding sites on VGAM180 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM180 host target RNA into VGAM180 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12085] It is appreciated that VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM180 host target genes. The mRNA of each one of this plurality of VGAM180 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM180 RNA, herein designated VGAM RNA, and which when bound by VGAM180 RNA causes inhibition of translation of respective one or more VGAM180 host target proteins.

[12086] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM180 gene, herein designated VGAM GENE, on one or more VGAM180 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12087] It is yet further appreciated that a function of VGAM180 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM180 correlate with, and may be deduced from, the identity of the host target genes which VGAM180 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12088] Nucleotide sequences of the VGAM180 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM180 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM180 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM180 are further described hereinbelow with reference to Table 1.

[12089] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM180 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM180 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[12090] As mentioned hereinabove with reference to Fig. 1, a function of VGAM180 gene, herein designated VGAM is inhibition of expression of VGAM180 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM180 correlate with, and may be deduced from, the identity of the target genes which VGAM180 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12091] Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila) (PDE4D, Accession XM_056815) is a VGAM180 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36434, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12092] A function of VGAM180 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila) (PDE4D, Accession

XM_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D has been established by previous studies. PDE4D is the mammalian homolog of 'dunce' in *Drosophila*. Flies deficient in this PDE display impairments of the central nervous system and reproductive functions (Dudai et al., 1976). Although only 1 dunce PDE has been described in the fly, 4 orthologous genes are present in mice, rats, and humans: PDE4A (OMIM Ref. No. 600126), PDE4B (OMIM Ref. No. 600127), PDE4C (OMIM Ref. No. 600128), and PDE4D. The encoded proteins share considerable homology in their catalytic and regulatory domains. To examine the role of a PDE in cAMP signaling in vivo, Jin et al. (1999) inactivated the PDE4D gene in mice. This isozyme is involved in feedback regulation of cAMP levels. Mice deficient in PDE4D exhibited delayed growth as well as reduced viability and female fertility. The decrease in fertility of the null female was caused by impaired ovulation and diminished sensitivity of the granulosa cells to gonadotropins. These pleiotropic phenotypes demonstrated

that PDE4D plays a critical role in cAMP signaling and that the activity of this isoenzyme is required for the regulation of growth and fertility. Muscarinic cholinergic signaling plays an essential role in the control of normal airway functions and in the development of pulmonary disease states, including asthma. Hansen et al. (2000) demonstrated that the airways of mice deficient in the cAMP-specific phosphodiesterase PDE4D were no longer responsive to cholinergic stimulation. Airway hyperreactivity that followed exposure to antigen was also abolished in PDE4D $-/-$ mice, despite apparently normal lung inflammatory infiltration. The loss of cholinergic responsiveness was specific to the airway, not observed in the heart, and was associated with a loss of signaling through muscarinic receptors with an inability to decrease cAMP accumulation. These findings demonstrated that the PDE4D gene plays an essential role in cAMP homeostasis and cholinergic stimulation of the airway, and in the development of hyperreactivity. In view of the therapeutic potentials of PDE4 inhibitors, the findings provided the rationale for novel strategies that target a single PDE isoenzyme.

[12093] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[12094] Jin, S.-L. C.; Richard, F. J.; Kuo, W.-P.; D'Ercole, A. J.; Conti, M. : Impaired growth and fertility of cAMP-specific phosphodiesterase PDE4D-deficient mice. Proc. Nat. Acad. Sci. 96: 11998-12003, 1999. ; and

[12095] Hansen, G.; Jin, S.-L. C.; Umetsu, D. T.; Conti, M. : Absence of muscarinic cholinergic airway responses in mice deficient in the cyclic nucleotide phosphodiesterase PDE4D. Proc. Nat. A.

[12096] Further studies establishing the function and utilities of PDE4D are found in John Hopkins OMIM database record ID 600129, and in cited publications numbered 1348-135 and 12445 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Replication Protein A1, 70kDa (RPA1, Accession NM_002945) is another VGAM180 host target gene. RPA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPA1 BINDING SITE, designated SEQ ID:8854, to the nucleotide sequence of VGAM180 RNA, herein designated

VGAM RNA, also designated SEQ ID:2891.

[12097] Another function of VGAM180 is therefore inhibition of Replication Protein A1, 70kDa (RPA1, Accession NM_002945), a gene which is required for simian virus 40 dna replication in vitro. it participates in a very early step in initiation. rp-a is a single-stranded dna-binding protein. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPA1. The function of RPA1 has been established by previous studies. Replication protein A (RPA) is a 3-subunit single-stranded DNA-binding protein that has been isolated from human cells and found to be essential for in vitro replication of the papovavirus SV40. Erdile et al. (1991) reported the sequence of a cDNA encoding the 70-kD subunit. The human cDNA directed production in E. coli of a 70-kD protein that reacted with a monoclonal antibody directed against the 70-kD subunit of the human protein. The recombinant subunit, purified from bacteria, exhibited single-stranded DNA-binding activity comparable to that of the complete RPA complex. It could substitute for the complete complex in stimulating the activity of DNA polymerase alpha-primase, but could not substitute for the complete complex in SV40 DNA

replication in vitro, suggesting an important functional role for the other subunits. Using PCR amplification of genomic DNA from rodent–human cell lines, Umbricht et al. (1993) mapped the gene for the 70–kD subunit to chromosome 17. By the same method, they mapped the genes for the 32–kD (OMIM Ref. No. 179836) and the 14–kD (OMIM Ref. No. 179837) subunits to chromosomes 1 and 7, respectively. Using a combination of PCR amplification of somatic cell hybrids and radiation hybrids containing chromosome 17 fragments, Umbricht et al. (1994) mapped RPA1 to 17p13.3. Gomes and Wold (1996) constructed a series of N–terminal deletions of RPA70 to explore the function of the protein. Their data indicated that RPA70 is composed of 3 functional domains: an N–terminal domain that is not required for single–stranded DNA binding or SV40 replication, a central DNA–binding domain, and a C–terminal domain that is essential for subunit interactions

[12098] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12099] Umbricht, C. B.; Griffin, C. A.; Hawkins, A. L.; Grzeschik, K. H.; O'Connell, P.; Leach, R.; Green, E. D.; Kelly, T. J. : High–

resolution genomic mapping of the three human replication protein A genes (RPA1, RPA2, and RPA3). Genomics 20: 249–257, 1994. ; and

[12100] Gomes, X. V.; Wold, M. S. : Functional domains of the 70–kilodalton subunit of human replication protein A. Biochemistry 35: 10558–10568, 1996.

[12101] Further studies establishing the function and utilities of RPA1 are found in John Hopkins OMIM database record ID 179835, and in cited publications numbered 1798–1799, 3280–328 and 1800–1802 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Son of Sevenless Homolog 2 (Drosophila) (SOS2, Accession XM_043720) is another VGAM180 host target gene. SOS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOS2 BINDING SITE, designated SEQ ID:34000, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12102] Another function of VGAM180 is therefore inhibition of Son of Sevenless Homolog 2 (Drosophila) (SOS2, Acces–

sion XM_043720). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOS2. TRAM (Accession NM_014294) is another VGAM180 host target gene. TRAM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAM BINDING SITE, designated SEQ ID:15593, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12103] Another function of VGAM180 is therefore inhibition of TRAM (Accession NM_014294). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAM. Tripartite Motif-containing 14 (TRIM14, Accession NM_014788) is another VGAM180 host target gene. TRIM14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TRIM14 BINDING SITE, designated SEQ ID:16668, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12104] Another function of VGAM180 is therefore inhibition of Tripartite Motif-containing 14 (TRIM14, Accession NM_014788), a gene which is composed of 3 zinc-binding domains and is involved in development and cell growth. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM14. The function of TRIM14 has been established by previous studies. TRIM proteins are composed of 3 zinc-binding domains, a RING, a B-box type 1, and a B-box type 2, followed by a coiled-coil region. They are involved in development and cell growth. By sequencing cDNAs randomly selected from a cDNA library derived from the human immature myeloid cell line KG-1, Nagase et al. (1995) identified a partial cDNA encoding TRIM14, which they called KIAA0129. The deduced 406-amino acid protein is 25% identical to RFP (OMIM Ref. No. 602165). Northern blot analysis revealed wide expression of KIAA0129 that was highest in liver but undetectable in skeletal muscle.

- [12105] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [12106] Nagase, T.; Seki, N.; Tanaka, A.; Ishikawa, K.; Nomura, N. : Prediction of the coding sequences of unidentified human genes. IV. The coding sequences of 40 new genes (KIAA0121–KIAA0160) deduced by analysis of cDNA clones from human cell line KG–1. DNA Res. 2: 167–174, 1995. ; and
- [12107] Reymond, A.; Meroni, G.; Fantozzi, A.; Merla, G.; Cairo, S.; Luzi, L.; Riganelli, D.; Zanaria, E.; Messali, S.; Cainarca, S.; Guffanti, A.; Minucci, S.; Pelicci, P. G.; Ballabio, A. : T.
- [12108] Further studies establishing the function and utilities of TRIM14 are found in John Hopkins OMIM database record ID 606556, and in cited publications numbered 10969 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tripartite Motif–containing 37 (TRIM37, Accession NM_015294) is another VGAM180 host target gene. TRIM37 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRIM37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen–

tarity of the nucleotide sequences of TRIM37 BINDING SITE, designated SEQ ID:17618, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12109] Another function of VGAM180 is therefore inhibition of Tripartite Motif-containing 37 (TRIM37, Accession NM_015294). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM37. Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM_012479) is another VGAM180 host target gene. YWHAG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YWHAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YWHAG BINDING SITE, designated SEQ ID:14857, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12110] Another function of VGAM180 is therefore inhibition of Tyrosine 3-monooxygenase/tryptophan

5-monooxygenase Activation Protein, Gamma Polypeptide (YWHAG, Accession NM_012479), a gene which mediates mitogenic signals of PDGF in vascular smooth muscle cells. Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YWHAG. The function of YWHAG has been established by previous studies. Members of the 14-3-3 protein family play an important role in signal transduction leading to mitosis and cellular proliferation (Morrison, 1994). For background information on 14-3-3 proteins, see 113508. Autieri et al. (1995, 1996) found that rat 14-3-3-gamma (YWHAG) is upregulated in injured rat carotid arteries and that YWHAG mRNA is upregulated in cytokine-stimulated human vascular smooth muscle cells (VSMC). Using PCR primers based on the rat YWHAG sequence to screen human VSMC, Autieri and Carbone (1999) isolated a cDNA encoding YWHAG. The deduced 246-amino acid protein, which shares 98% sequence identity with the rat sequence, has preserved 14-3-3 family signature motifs, a predicted annexin motif, and several potential phosphorylation sites but not the CDK2 (OMIM Ref. No. 116953) phosphorylation motif. By EST database searching, Horie et al. (1999) also obtained

a cDNA encoding YWHAG, which they found to be 100% identical to the 247-amino acid rat sequence. Northern blot analysis revealed ubiquitous expression of a 3.8-kb YWHAG transcript that is relatively strong in brain, skeletal muscle, and heart but weak in peripheral blood leukocytes. By SDS-PAGE and autoradiographic analysis, Autieri and Carbone (1999) found that YWHAG is expressed and phosphorylated by activation with platelet-derived growth factor (OMIM Ref. No. 190040) and other activators of several isoforms of protein kinase C (PKC; e.g., 176960). Inhibitors of PKC block YWHAG phosphorylation. Western blot analysis showed that YWHAG interacts with PKC and with RAF1 (OMIM Ref. No. 164760).

[12111] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12112] Autieri, M. V.; Carbone, C. J. : 14-3-3-Gamma interacts with and is phosphorylated by multiple protein kinase C isoforms in PDGF-stimulated human vascular smooth muscle cells. DNA Cell Biol. 18: 555-564, 1999. ; and

[12113] Horie, M.; Suzuki, M.; Takahashi, E.; Tanigami, A. : Cloning, expression, and chromosomal mapping of the human 14-3-3gamma gene (YWHAG) to 7q11.23. Ge-

nomics 60: 241–243, 1999.

[12114] Further studies establishing the function and utilities of YWHAG are found in John Hopkins OMIM database record ID 605356, and in cited publications numbered 618 and 6629–6632 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Basic Leucine Zipper Nuclear Factor 1 (JEM–1) (BLZF1, Accession NM_003666) is another VGAM180 host target gene. BLZF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BLZF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BLZF1 BINDING SITE, designated SEQ ID:9751, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12115] Another function of VGAM180 is therefore inhibition of Basic Leucine Zipper Nuclear Factor 1 (JEM–1) (BLZF1, Accession NM_003666). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BLZF1. DKFZP564D172 (Accession NM_032042) is another VGAM180 host target gene. DKFZP564D172 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564D172 BINDING SITE, designated SEQ ID:25752, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12116] Another function of VGAM180 is therefore inhibition of DKFZP564D172 (Accession NM_032042). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D172. FLJ10154 (Accession NM_018011) is another VGAM180 host target gene. FLJ10154 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10154, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10154 BINDING SITE, designated SEQ ID:19746, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12117] Another function of VGAM180 is therefore inhibition of

FLJ10154 (Accession NM_018011). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10154. FLJ11996 (Accession NM_024976) is another VGAM180 host target gene. FLJ11996 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ11996, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11996 BINDING SITE, designated SEQ ID:24533, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12118] Another function of VGAM180 is therefore inhibition of FLJ11996 (Accession NM_024976). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11996. KIAA1432 (Accession XM_039698) is another VGAM180 host target gene. KIAA1432 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA1432 BINDING SITE, designated SEQ ID:33157, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12119] Another function of VGAM180 is therefore inhibition of KIAA1432 (Accession XM_039698). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1432. KIAA1946 (Accession XM_092459) is another VGAM180 host target gene. KIAA1946 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1946 BINDING SITE, designated SEQ ID:40121, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12120] Another function of VGAM180 is therefore inhibition of KIAA1946 (Accession XM_092459). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1946. Spir-1 (Accession XM_035640) is another

VGAM180 host target gene. Spir-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Spir-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Spir-1 BINDING SITE, designated SEQ ID:32308, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12121] Another function of VGAM180 is therefore inhibition of Spir-1 (Accession XM_035640). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Spir-1. Trinucleotide Repeat Containing 6 (TNRC6, Accession XM_047123) is another VGAM180 host target gene. TNRC6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNRC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNRC6 BINDING SITE, designated SEQ ID:34900, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ

ID:2891.

[12122] Another function of VGAM180 is therefore inhibition of Trinucleotide Repeat Containing 6 (TNRC6, Accession XM_047123). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNRC6. LOC143098 (Accession XM_084421) is another VGAM180 host target gene. LOC143098 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143098 BINDING SITE, designated SEQ ID:37576, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12123] Another function of VGAM180 is therefore inhibition of LOC143098 (Accession XM_084421). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143098. LOC220883 (Accession XM_166076) is another VGAM180 host target gene. LOC220883 BINDING SITE is HOST TARGET binding site found in the 3` un-

translated region of mRNA encoded by LOC220883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220883 BINDING SITE, designated SEQ ID:43850, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12124] Another function of VGAM180 is therefore inhibition of LOC220883 (Accession XM_166076). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220883. LOC253981 (Accession XM_171064) is another VGAM180 host target gene. LOC253981 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253981, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253981 BINDING SITE, designated SEQ ID:45867, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12125] Another function of VGAM180 is therefore inhibition of LOC253981 (Accession XM_171064). Accordingly, utilities

of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253981. LOC257464 (Accession XM_116972) is another VGAM180 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43168, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12126] Another function of VGAM180 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. LOC55885 (Accession NM_018640) is another VGAM180 host target gene. LOC55885 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC55885, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC55885 BINDING SITE, designated SEQ ID:20712, to the nucleotide sequence of VGAM180 RNA, herein designated VGAM RNA, also designated SEQ ID:2891.

[12127] Another function of VGAM180 is therefore inhibition of LOC55885 (Accession NM_018640). Accordingly, utilities of VGAM180 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55885. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 181 (VGAM181) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12128] VGAM181 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM181 was detected is described hereinabove with reference to Figs. 1–8.

[12129] VGAM181 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12130] VGAM181 gene encodes a VGAM181 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM181 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM181 precursor RNA is designated SEQ ID:167, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:167 is located at position 284231 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12131] VGAM181 precursor RNA folds onto itself, forming VGAM181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12132] An enzyme complex designated DICER COMPLEX, `dices` the VGAM181 folded precursor RNA into VGAM181 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM181 RNA is designated SEQ ID:2892, and is provided hereinbelow with reference to the sequence listing part.

[12133] VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM181 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12134] VGAM181 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM181 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM181 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12135] The complementary binding of VGAM181 RNA, herein designated VGAM RNA, to host target binding sites on VGAM181 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM181 host target RNA into VGAM181 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12136] It is appreciated that VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM181 host target genes. The mRNA of each one of this plurality of VGAM181 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM181 RNA, herein designated VGAM RNA, and which when bound by VGAM181 RNA causes inhibition of translation of respective one or more VGAM181 host target proteins.

[12137] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM181 gene, herein designated VGAM GENE, on one or more VGAM181 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12138] It is yet further appreciated that a function of VGAM181 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM181 correlate with, and may be deduced from, the identity of the host target genes which VGAM181 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12139] Nucleotide sequences of the VGAM181 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM181 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM181 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM181 are further described hereinbelow with reference to Table 1.

[12140] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM181 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM181 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12141] As mentioned hereinabove with reference to Fig. 1, a function of VGAM181 gene, herein designated VGAM is inhibition of expression of VGAM181 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM181 correlate with, and may be deduced from, the identity of the target genes which VGAM181 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12142] Phosphatidylinositol Glycan, Class C (PIGC, Accession NM_002642) is a VGAM181 host target gene. PIGC BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PIGC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIGC BINDING SITE, designated SEQ ID:8502, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM

RNA, also designated SEQ ID:2892.

[12143] A function of VGAM181 is therefore inhibition of Phosphatidylinositol Glycan, Class C (PIGC, Accession NM_002642), a gene which is involved in the first step of gpi biosynthesis. Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIGC. The function of PIGC has been established by previous studies. Many eukaryotic membrane proteins are anchored to membranes via glycosylphosphatidylinositol (GPI) anchors. GPI anchoring is a posttranslational modification occurring in the endoplasmic reticulum (ER). The first step of GPI biosynthesis requires at least 3 genes termed PIGA (OMIM Ref. No. 311770), PIGH (OMIM Ref. No. 600154), and PIGC. Inoue et al. (1996) cloned a human homolog of GPI2 and showed that it is PIGC. PIGC encodes a 297-amino acid polypeptide that is 20% identical to yeast GPI2. This gene, when transfected into human cells mutant for PIGC activity, restored proper GPI anchoring. Using immunolocalization, they found human PIGC protein to be present primarily in the ER in transfected cells Using immunoprecipitation experiments, Watanabe et al. (1998) demonstrated that PIGQ (OMIM Ref. No. 605754) associates specifically

with PIGA, PIGC, and PIGH and that all 4 proteins form a complex that has GPI-GlcNAc transferase (GPI-GnT) activity in vitro.

[12144] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12145] Inoue, N.; Watanabe, R.; Takeda, J.; Kinoshita, T. : PIG-C, one of the three human genes involved in the first step of glycosylphosphatidylinositol biosynthesis is a homologue of *Saccharomyces cerevisiae* GPI2. *Biochem. Biophys. Res. Commun.* 226: 193-199, 1996. ; and

[12146] Watanabe, R.; Inoue, N.; Westfall, B.; Taron, C. H.; Orlean, P.; Takeda, J.; Kinoshita, T. : The first step of glycosylphosphatidylinositol biosynthesis is mediated by a complex of PIG-A.

[12147] Further studies establishing the function and utilities of PIGC are found in John Hopkins OMIM database record ID 601730, and in cited publications numbered 930 and 9321 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10408 (Accession NM_018088) is another VGAM181 host target gene. FLJ10408 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded

by FLJ10408, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10408 BINDING SITE, designated SEQ ID:19851, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, also designated SEQ ID:2892.

[12148] Another function of VGAM181 is therefore inhibition of FLJ10408 (Accession NM_018088). Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10408. KIAA0350 (Accession XM_028332) is another VGAM181 host target gene. KIAA0350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0350 BINDING SITE, designated SEQ ID:30660, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, also designated SEQ ID:2892.

[12149] Another function of VGAM181 is therefore inhibition of KIAA0350 (Accession XM_028332). Accordingly, utilities

of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0350. KIAA0892 (Accession XM_048457) is another VGAM181 host target gene. KIAA0892 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0892, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0892 BINDING SITE, designated SEQ ID:35174, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, also designated SEQ ID:2892.

[12150] Another function of VGAM181 is therefore inhibition of KIAA0892 (Accession XM_048457). Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0892. TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256) is another VGAM181 host target gene. TRAF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of TRAF3 BINDING SITE, designated SEQ ID:30039, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, also designated SEQ ID:2892.

[12151] Another function of VGAM181 is therefore inhibition of TNF Receptor-associated Factor 3 (TRAF3, Accession XM_007256). Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF3. LOC150245 (Accession XM_097843) is another VGAM181 host target gene. LOC150245 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150245 BINDING SITE, designated SEQ ID:41159, to the nucleotide sequence of VGAM181 RNA, herein designated VGAM RNA, also designated SEQ ID:2892.

[12152] Another function of VGAM181 is therefore inhibition of LOC150245 (Accession XM_097843). Accordingly, utilities of VGAM181 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC150245. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 182 (VGAM182) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12153] VGAM182 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM182 was detected is described hereinabove with reference to Figs. 1–8.

[12154] VGAM182 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12155] VGAM182 gene encodes a VGAM182 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM182 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM182 precursor RNA is designated SEQ ID:168, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:168 is located at position 31462 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12156] VGAM182 precursor RNA folds onto itself, forming VGAM182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12157] An enzyme complex designated DICER COMPLEX, `dices` the VGAM182 folded precursor RNA into VGAM182 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM182 RNA is designated SEQ ID:2893, and is provided hereinbelow with reference to the sequence

listing part.

[12158] VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM182 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12159] VGAM182 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM182 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM182 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12160] The complementary binding of VGAM182 RNA, herein designated VGAM RNA, to host target binding sites on VGAM182 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM182 host target RNA into VGAM182 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12161] It is appreciated that VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM182 host target genes. The mRNA of each one of this plurality of VGAM182 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM182 RNA, herein designated VGAM

RNA, and which when bound by VGAM182 RNA causes inhibition of translation of respective one or more VGAM182 host target proteins.

[12162] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM182 gene, herein designated VGAM GENE, on one or more VGAM182 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12163] It is yet further appreciated that a function of VGAM182 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM182 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM182 correlate with, and may be deduced from, the identity of the host target genes which VGAM182 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12164] Nucleotide sequences of the VGAM182 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM182 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM182 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM182 are further described hereinbelow with reference to Table 1.

[12165] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM182 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM182 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12166] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM182 gene, herein designated VGAM is inhibition of expression of VGAM182 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM182 correlate with, and may be deduced from, the identity of the target genes which VGAM182 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12167] Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719) is a VGAM182 host target gene. CACNA1C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CACNA1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA1C BINDING SITE, designated SEQ ID:6383, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12168] A function of VGAM182 is therefore inhibition of Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719), a gene which is alpha-1 subunit of DHP-sensitive calcium channels from cardiac muscle and the brain. Accordingly, utilities of

VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA1C. The function of CACNA1C has been established by previous studies. Activation of voltage-sensitive calcium channels by membrane depolarization triggers key cellular responses such as contraction, secretion, excitation, and electrical signaling (Tsien et al., 1991). The L-type currents produced by voltage-sensitive calcium channels are blocked by 1,4-dihydropyridine (DHP) derivatives; thus, the channels responsible for these currents are referred to as DHP-sensitive. The skeletal muscle DHP-sensitive calcium channel is a complex of 5 subunits: alpha-1, alpha-2, beta, gamma, and delta. The DHP-sensitive calcium channels from cardiac muscle and the brain have pharmacologic and electrophysiologic properties that differ from those of the skeletal muscle channel. Powers et al. (1991) isolated a clone for the human CCHL1A1 gene and partially sequenced it. Oligonucleotides based on the human sequence were constructed and used in PCR to amplify specifically this human gene in human-rodent somatic cell hybrids. In this way, the gene was assigned to 12pter-p12. Using a dinucleotide repeat for linkage analysis in the CEPH panel of families, Powers et al. (1992)

narrowed the assignment to 12pter–p13.2. The data placed CACNL1A1 distal to PRB1 (OMIM Ref. No. 180989). By study of somatic cell hybrids, Sun et al. (1992) likewise assigned the CACNL1A1 gene to 12pter–p13. (The gene is also symbolized CACNA1C and CCHL1A1.) Schultz et al. (1993) localized the CCHL1A1 gene to 12p13.3 by study of a 12p somatic cell hybrid mapping panel and by fluorescence in situ hybridization. Animal model experiments lend further support to the function of CACNA1C. Valenzuela et al. (1997) generated knockout mice lacking both forms of Go–alpha (OMIM Ref. No. 139311) by homologous recombination and studied the muscarinic regulation of calcium channels in cardiac muscles in Go–alpha –/– mice and controls. There was no difference in the effect of isoproterenol on the L–type voltage–dependent calcium channel in ventricular myocytes of both groups, but the inhibitory effect of carbamylcholine was almost completely abolished in the Go–alpha –/– group. This demonstrated that, in the heart, Go–alpha is specifically required for transmission of signals from the muscarinic receptor to the L–type voltage–dependent calcium channel.

[12169] It is appreciated that the abovementioned animal model for CACNA1C is acknowledged by those skilled in the art

as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[12170] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12171] Valenzuela, D.; Han, X.; Mende, U.; Fankhauser, C.; Mashimo, H.; Huang, P.; Pfeffer, J.; Neer, E. J.; Fishman, M. C. : G-alpha-o is necessary for muscarinic regulation of Ca(2+) channels in mouse heart. Proc. Nat. Acad. Sci. 94: 1727-2732, 1997. ; and

[12172] Tsien, R. W.; Ellinor, P. T.; Horne, W. A. : Molecular diversity of voltage-dependent Ca(2+) channels. Trends Pharm. Sci. 12: 349-354, 1991.

[12173] Further studies establishing the function and utilities of CACNA1C are found in John Hopkins OMIM database record ID 114205, and in sited publications numbered 179, 10478-4700, 10079-4702, 4850-4849, 361 and 10270 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ11101 (Accession NM_018322) is another VGAM182 host target gene. FLJ11101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11101, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11101 BINDING SITE, designated SEQ ID:20316, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12174] Another function of VGAM182 is therefore inhibition of FLJ11101 (Accession NM_018322). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11101. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM182 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FYCO1 BINDING SITE, designated SEQ ID:23715, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12175] Another function of VGAM182 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Ac-

cession NM_024513). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Makorin, Ring Finger Protein, 1 (MKRN1, Accession NM_013446) is another VGAM182 host target gene. MKRN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKRN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN1 BINDING SITE, designated SEQ ID:15113, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12176] Another function of VGAM182 is therefore inhibition of Makorin, Ring Finger Protein, 1 (MKRN1, Accession NM_013446). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN1. Makorin, Ring Finger Protein, 4 (MKRN4, Accession NM_030757) is another VGAM182 host target gene. MKRN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKRN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKRN4 BINDING SITE, designated SEQ ID:25042, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12177] Another function of VGAM182 is therefore inhibition of Makorin, Ring Finger Protein, 4 (MKRN4, Accession NM_030757). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKRN4. MTO1 (Accession NM_133645) is another VGAM182 host target gene. MTO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTO1 BINDING SITE, designated SEQ ID:28603, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12178] Another function of VGAM182 is therefore inhibition of MTO1 (Accession NM_133645). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTO1.

Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM_002714) is another VGAM182 host target gene. PPP1R10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R10 BINDING SITE, designated SEQ ID:8574, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12179] Another function of VGAM182 is therefore inhibition of Protein Phosphatase 1, Regulatory Subunit 10 (PPP1R10, Accession NM_002714). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R10. STRIN (Accession NM_016271) is another VGAM182 host target gene. STRIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRIN BINDING SITE, designated SEQ ID:18398,

to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12180] Another function of VGAM182 is therefore inhibition of STRIN (Accession NM_016271). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRIN. Testis-specific Kinase 2 (TESK2, Accession XM_032399) is another VGAM182 host target gene. TESK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TESK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK2 BINDING SITE, designated SEQ ID:31650, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12181] Another function of VGAM182 is therefore inhibition of Testis-specific Kinase 2 (TESK2, Accession XM_032399). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TESK2. LOC150481 (Accession XM_086929) is another VGAM182 host target gene. LOC150481 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LOC150481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150481 BINDING SITE, designated SEQ ID:38983, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12182] Another function of VGAM182 is therefore inhibition of LOC150481 (Accession XM_086929). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150481. LOC158191 (Accession XM_088505) is another VGAM182 host target gene. LOC158191 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158191, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158191 BINDING SITE, designated SEQ ID:39759, to the nucleotide sequence of VGAM182 RNA, herein designated VGAM RNA, also designated SEQ ID:2893.

[12183] Another function of VGAM182 is therefore inhibition of

LOC158191 (Accession XM_088505). Accordingly, utilities of VGAM182 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158191. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 183 (VGAM183) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12184] VGAM183 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM183 was detected is described hereinabove with reference to Figs. 1–8.

[12185] VGAM183 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12186] VGAM183 gene encodes a VGAM183 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM183 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM183 precursor RNA is designated SEQ ID:169, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:169 is located at position 93258 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12187] VGAM183 precursor RNA folds onto itself, forming VGAM183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12188] An enzyme complex designated DICER COMPLEX, `dices` the VGAM183 folded precursor RNA into VGAM183 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 66%) nucleotide sequence of VGAM183 RNA is designated SEQ ID:2894, and is provided hereinbelow with reference to the sequence listing part.

[12189] VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM183 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[12190] VGAM183 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM183 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM183 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12191] The complementary binding of VGAM183 RNA, herein designated VGAM RNA, to host target binding sites on VGAM183 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM183 host target RNA into VGAM183 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12192] It is appreciated that VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM183 host target genes. The mRNA of each one of this plurality of VGAM183 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM183 RNA, herein designated VGAM RNA, and which when bound by VGAM183 RNA causes inhibition of translation of respective one or more VGAM183 host target proteins.

[12193] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM183 gene, herein designated VGAM GENE, on one or more VGAM183 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12194] It is yet further appreciated that a function of VGAM183 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM183 correlate with, and may be deduced from, the identity of the host target genes which VGAM183 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12195] Nucleotide sequences of the VGAM183 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM183 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM183 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM183 are further described hereinbelow with reference to Table 1.

[12196] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM183 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM183 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[12197] As mentioned hereinabove with reference to Fig. 1, a function of VGAM183 gene, herein designated VGAM is inhibition of expression of VGAM183 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM183 correlate with, and may be deduced from, the identity of the target genes which VGAM183 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12198] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 6 (B4GALT6, Accession XM_008799) is a VGAM183 host target gene. B4GALT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT6 BINDING SITE, designated SEQ ID:30091, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12199] A function of VGAM183 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypep-

tide 6 (B4GALT6, Accession XM_008799). Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT6. Orthopedia Homolog (Drosophila) (OTP, Accession NM_032109) is another VGAM183 host target gene. OTP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OTP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OTP BINDING SITE, designated SEQ ID:25803, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12200] Another function of VGAM183 is therefore inhibition of Orthopedia Homolog (Drosophila) (OTP, Accession NM_032109), a gene which involves in the development of the forebrain and spinal cord. Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OTP. The function of OTP has been established by previous studies. Homeodomain genes are helix–turn–helix transcription factors that play key roles in the specification of cell fates. In the central nervous system, homeodomain genes not

only position cells along an axis, but also specify cell migration patterns and may influence axonal connectivity. In an effort to identify novel homeodomain genes involved in the development of the human central nervous system, Lin et al. (1999) cloned, characterized, and mapped the human homolog of the murine homeodomain gene *Orthopedia* (*Otp*), whose product is found in multiple cell groups within the mouse hypothalamus, amygdala, and brain stem. The human OTP cDNA encodes a protein of 325 amino acids. The deduced amino acid sequence is 99% homologous to mouse *Otp* and demonstrated a high degree of conservation when compared to sea urchin and *Drosophila* *Otp* proteins. A single putative OTP gene product was found in 17-week human fetal brain tissue by Western blot analysis using a novel polyclonal antibody raised against a conserved 13-amino acid sequence in the C terminus of the OTP protein. Expression in the developing human hypothalamus was confirmed by immunohistochemistry. Lin et al. (1999) mapped the human OTP gene to chromosome 5q13.3 using analysis of a radiation hybrid panel and by fluorescence in situ hybridization. Animal model experiments lend further support to the function of OTP. Acampora et al. (1999) generated mice defi-

cient in Otp by homologous recombination. Homozygous Otp $-/-$ mice died soon after birth and displayed progressive impairment of crucial neuroendocrine developmental events such as reduced cell proliferation, abnormal cell migration, and failure in terminal differentiation of the parvocellular and magnocellular neurons of the anterior periventricular, paraventricular, supraoptic, and arcuate nuclei. Acampora et al. (1999) suggested that Otp and Sim1 (OMIM Ref. No. 603128) are required to maintain Brn2 (OMIM Ref. No. 600494) expression which, in turn, is required for neuronal cell lineages secreting oxytocin (OMIM Ref. No. 167050), arginine vasopressin (OMIM Ref. No. 192340), and corticotropin-releasing (OMIM Ref. No. 122560) hormones.

[12201] It is appreciated that the abovementioned animal model for OTP is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12202] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12203] Acampora, D.; Postiglione, M. P.; Avantaggiato, V.; Di Bonito, M.; Vaccarino, F. M.; Michaud, J.; Simeone, A. :

Progressive impairment of developing neuroendocrine cell lineages in the hypothalamus of mice lacking the Orthopedia gene. Genes Dev. 13: 2787–2800, 1999. ; and

[12204] Lin, X.; State, M. W.; Vaccarino, F. M.; Greally, J.; Hass, M.; Leckman, J. F. : Identification, chromosomal assignment, and expression analysis of the human homeodomain-containing gene.

[12205] Further studies establishing the function and utilities of OTP are found in John Hopkins OMIM database record ID 604529, and in cited publications numbered 7088–7089 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.FLJ20160 (Accession NM_017694) is another VGAM183 host target gene. FLJ20160 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20160 BINDING SITE, designated SEQ ID:19257, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12206] Another function of VGAM183 is therefore inhibition of

FLJ20160 (Accession NM_017694). Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20160. High-mobility Group (nonhistone chromosomal) Protein 17-like 1 (HMG17L1, Accession NM_021024) is another VGAM183 host target gene. HMG17L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HMG17L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HMG17L1 BINDING SITE, designated SEQ ID:22015, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12207] Another function of VGAM183 is therefore inhibition of High-mobility Group (nonhistone chromosomal) Protein 17-like 1 (HMG17L1, Accession NM_021024). Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HMG17L1. LOC123283 (Accession XM_071829) is another VGAM183 host target gene. LOC123283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC123283, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123283 BINDING SITE, designated SEQ ID:37423, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12208] Another function of VGAM183 is therefore inhibition of LOC123283 (Accession XM_071829). Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123283. LOC143524 (Accession XM_084559) is another VGAM183 host target gene. LOC143524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143524 BINDING SITE, designated SEQ ID:37629, to the nucleotide sequence of VGAM183 RNA, herein designated VGAM RNA, also designated SEQ ID:2894.

[12209] Another function of VGAM183 is therefore inhibition of LOC143524 (Accession XM_084559). Accordingly, utilities of VGAM183 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC143524. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 184 (VGAM184) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12210] VGAM184 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM184 was detected is described hereinabove with reference to Figs. 1–8.

[12211] VGAM184 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12212] VGAM184 gene encodes a VGAM184 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM184 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM184 precursor RNA is designated SEQ

ID:170, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:170 is located at position 166001 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12213] VGAM184 precursor RNA folds onto itself, forming VGAM184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12214] An enzyme complex designated DICER COMPLEX, `dices` the VGAM184 folded precursor RNA into VGAM184 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM184 RNA is designated SEQ ID:2895, and

is provided hereinbelow with reference to the sequence listing part.

[12215] VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM184 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12216] VGAM184 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM184 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM184 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12217] The complementary binding of VGAM184 RNA, herein designated VGAM RNA, to host target binding sites on VGAM184 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM184 host target RNA into VGAM184 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12218] It is appreciated that VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM184 host target genes. The mRNA of each one of this plurality of VGAM184 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM184 RNA, herein designated VGAM RNA, and which when bound by VGAM184 RNA causes inhibition of translation of respective one or more VGAM184 host target proteins.

[12219] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM184 gene, herein designated VGAM GENE, on one or more VGAM184 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12220] It is yet further appreciated that a function of VGAM184 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM184 correlate with, and may be deduced from, the identity of the host target genes which VGAM184 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12221] Nucleotide sequences of the VGAM184 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM184 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM184 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM184 are further described hereinbelow with reference to Table 1.

[12222] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM184 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM184 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12223] As mentioned hereinabove with reference to Fig. 1, a function of VGAM184 gene, herein designated VGAM is inhibition of expression of VGAM184 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM184 correlate with, and may be deduced from, the identity of the target genes which VGAM184 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12224] D10S170 (Accession NM_005436) is a VGAM184 host target gene. D10S170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D10S170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D10S170 BINDING SITE, designated SEQ ID:11917, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12225] A function of VGAM184 is therefore inhibition of D10S170 (Accession NM_005436), a gene which may provide a structural basis for generation of RET/PTC1 rearrangement. Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with D10S170. The function of D10S170 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM142. Dihydropyrimidine Dehydrogenase (DPYD, Accession XM_017469) is another VGAM184 host target gene. DPYD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYD BINDING SITE, designated SEQ ID:30315, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12226] Another function of VGAM184 is therefore inhibition of Dihydropyrimidine Dehydrogenase (DPYD, Accession XM_017469). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYD. V-myb Myeloblastosis Viral Oncogene Homolog (avian)-like 1 (MYBL1, Accession XM_034274) is another VGAM184 host target gene. MYBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MYBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYBL1 BINDING SITE, designated SEQ ID:32040, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12227] Another function of VGAM184 is therefore inhibition of V-myb Myeloblastosis Viral Oncogene Homolog (avian)-like 1 (MYBL1, Accession XM_034274), a gene which could have a role in the proliferation and/or differentiation of neurogenic, spermatogenic and b-lymphoid cells. Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYBL1. The function of MYBL1 has been established by previous studies. Nomura et al. (1988) isolated and characterized cDNA clones for 2 human MYB-related genes, AMYB and BMYB (OMIM Ref. No. 601415). Using probes in Southern blot analysis of rodent-human hybrid DNAs, Barletta et al. (1991) localized the MYBL1 locus to 8cen-q22 and refined the localization to 8q22-q23 by in situ hybridization. Takahashi et al. (1995) found that MYBL1 mRNA is expressed mainly in testis and peripheral

blood leukocytes. AMYB could activate transcription from the promoter-containing MYB-binding sites in all cells examined. In addition to the 2 domains (a DNA-binding domain and a transcriptional activation domain), 2 negative regulatory domains were identified in the MYBL1 gene.

These results indicated that the gene functions as a transcriptional activator and that the regulatory mechanism of gene activity is similar to that of the MYB (OMIM Ref. No. 189990) gene.

[12228] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12229] Nomura, N.; Takahashi, M.; Matsui, M.; Ishii, S.; Date, T.; Sasamoto, S.; Ishizaki, R. : Isolation of human cDNA clones of MYB-related genes, A-MYB and B-MYB. *Nucleic Acids Res.* 16: 11075-11089, 1988. ; and

[12230] Takahashi, T.; Nakagoshi, H.; Sarai, A.; Nomura, N.; Yamamoto, T.; Ishii, S. : Human A-myb gene encodes a transcriptional activator containing the negative regulatory domains. *FEBS Lett.*

[12231] Further studies establishing the function and utilities of MYBL1 are found in John Hopkins OMIM database record ID 159405, and in cited publications numbered

11008–11010 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ornithine Carbamoyltransferase (OTC, Accession NM_000531) is another VGAM184 host target gene. OTC BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by OTC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OTC BINDING SITE, designated SEQ ID:6132, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12232] Another function of VGAM184 is therefore inhibition of Ornithine Carbamoyltransferase (OTC, Accession NM_000531). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OTC. CASPR3 (Accession NM_033655) is another VGAM184 host target gene. CASPR3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CASPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CASPR3 BINDING SITE, designated SEQ ID:27387, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12233] Another function of VGAM184 is therefore inhibition of CASPR3 (Accession NM_033655). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASPR3. KIAA1046 (Accession NM_014928) is another VGAM184 host target gene. KIAA1046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1046 BINDING SITE, designated SEQ ID:17218, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12234] Another function of VGAM184 is therefore inhibition of KIAA1046 (Accession NM_014928). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1046. Voltage-dependent Anion Channel 3 (VDAC3,

Accession NM_005662) is another VGAM184 host target gene. VDAC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VDAC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VDAC3 BINDING SITE, designated SEQ ID:12201, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12235] Another function of VGAM184 is therefore inhibition of Voltage-dependent Anion Channel 3 (VDAC3, Accession NM_005662). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VDAC3. LOC143888 (Accession XM_084669) is another VGAM184 host target gene. LOC143888 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143888, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143888 BINDING SITE, designated SEQ ID:37664, to the nucleotide sequence of

VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12236] Another function of VGAM184 is therefore inhibition of LOC143888 (Accession XM_084669). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143888. LOC149271 (Accession XM_086475) is another VGAM184 host target gene. LOC149271 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149271 BINDING SITE, designated SEQ ID:38672, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12237] Another function of VGAM184 is therefore inhibition of LOC149271 (Accession XM_086475). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149271. LOC149910 (Accession XM_086699) is another VGAM184 host target gene. LOC149910 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC149910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149910 BINDING SITE, designated SEQ ID:38825, to the nucleotide sequence of VGAM184 RNA, herein designated VGAM RNA, also designated SEQ ID:2895.

[12238] Another function of VGAM184 is therefore inhibition of LOC149910 (Accession XM_086699). Accordingly, utilities of VGAM184 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149910. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 185 (VGAM185) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12239] VGAM185 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM185 was detected is described hereinabove with reference to Figs. 1–8.

[12240] VGAM185 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12241] VGAM185 gene encodes a VGAM185 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM185 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM185 precursor RNA is designated SEQ ID:171, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:171 is located at position 283443 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12242] VGAM185 precursor RNA folds onto itself, forming VGAM185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[12243] An enzyme complex designated DICER COMPLEX, `dices` the VGAM185 folded precursor RNA into VGAM185 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM185 RNA is designated SEQ ID:2896, and is provided hereinbelow with reference to the sequence listing part.

[12244] VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM185 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12245] VGAM185 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM185 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM185 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[12246] The complementary binding of VGAM185 RNA, herein designated VGAM RNA, to host target binding sites on VGAM185 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM185 host target RNA into VGAM185 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12247] It is appreciated that VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM185 host target genes. The mRNA of each one of this plurality of VGAM185 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM185 RNA, herein designated VGAM RNA, and which when bound by VGAM185 RNA causes in-

hibition of translation of respective one or more VGAM185 host target proteins.

[12248] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM185 gene, herein designated VGAM GENE, on one or more VGAM185 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12249] It is yet further appreciated that a function of VGAM185 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM185 include diagnosis, prevention and

treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM185 correlate with, and may be deduced from, the identity of the host target genes which VGAM185 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [12250] Nucleotide sequences of the VGAM185 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM185 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM185 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM185 are further described hereinbelow with reference to Table 1.
- [12251] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM185 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM185 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [12252] As mentioned hereinabove with reference to Fig. 1, a function of VGAM185 gene, herein designated VGAM is

inhibition of expression of VGAM185 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM185 correlate with, and may be deduced from, the identity of the target genes which VGAM185 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12253] Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400) is a VGAM185 host target gene. PLA2G2D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G2D BINDING SITE, designated SEQ ID:14770, to the nucleotide sequence of VGAM185 RNA, herein designated VGAM RNA, also designated SEQ ID:2896.

[12254] A function of VGAM185 is therefore inhibition of Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400), a gene which is involved in phospholipid digestion, remodeling of cell membranes, and host defense, as well as pathophysiologic processes. Accordingly, utilities of VGAM185 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with PLA2G2D. The function of PLA2G2D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74.DKFZp761D221 (Accession NM_032291) is another VGAM185 host target gene. DKFZp761D221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761D221 BINDING SITE, designated SEQ ID:26059, to the nucleotide sequence of VGAM185 RNA, herein designated VGAM RNA, also designated SEQ ID:2896.

[12255] Another function of VGAM185 is therefore inhibition of DKFZp761D221 (Accession NM_032291). Accordingly, utilities of VGAM185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D221. KIAA0632 (Accession NM_015545) is another VGAM185 host target gene. KIAA0632 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0632, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0632 BINDING SITE, designated SEQ ID:17807, to the nucleotide sequence of VGAM185 RNA, herein designated VGAM RNA, also designated SEQ ID:2896.

[12256] Another function of VGAM185 is therefore inhibition of KIAA0632 (Accession NM_015545). Accordingly, utilities of VGAM185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0632. NDRG Family Member 4 (NDRG4, Accession NM_020465) is another VGAM185 host target gene. NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NDRG4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NDRG4 BINDING SITE1 and NDRG4 BINDING SITE2, designated SEQ ID:21700 and SEQ ID:23215 respectively, to the nucleotide sequence of VGAM185 RNA, herein designated VGAM RNA, also designated SEQ ID:2896.

[12257] Another function of VGAM185 is therefore inhibition of

NDRG Family Member 4 (NDRG4, Accession NM_020465). Accordingly, utilities of VGAM185 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NDRG4. Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM_012126) is another VGAM186 host target gene. CHST5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHST5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST5 BINDING SITE, designated SEQ ID:14441, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12258] Another function of VGAM186 is therefore inhibition of Carbohydrate (N-acetylglucosamine 6-O) Sulfotransferase 5 (CHST5, Accession NM_012126), a gene which may be involved in sulfation of glycoproteins and proteoglycans. Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST5. The function of CHST5 has been established by previous studies. The carbohydrates of gly-

coconjugates are highly diverse structures with variation in monosaccharide composition, glycosidic linkage positions, and branching of chains. Further diversity is added by the covalent addition of sulfate moieties to particular hydroxyl groups and amino groups of saccharides. The sulfate modifications of glycoproteins can be extensive in amount and frequently occur at high density. They can have a profound effect on the physiochemical properties of the glycoconjugates, at least in part through the addition of negative charge. Carbohydrate sulfation plays a critical role in many biologic processes. The GST family of sulfotransferases includes CHST1 (OMIM Ref. No. 603797), CHST2 (OMIM Ref. No. 603798), CHST3 (OMIM Ref. No. 603799), and LSST. These enzymes are 6-O-sulfotransferases, which add sulfate to C6 of galactose (Gal), N-acetylgalactosamine (OMIM Ref. No. GalNAc), or N-acetylglucosamine (OMIM Ref. No. GlcNAc). By searching an EST database with the sequences of CHST1 and LSST, Lee et al. (1999) identified nonoverlapping ESTs encoding CHST5, which they called IGlcNAc6ST. They isolated additional CHST5 ESTs and assembled a complete CHST5 coding sequence. The deduced 390-amino acid CHST5 protein is predicted to be a type II transmembrane

protein, with an N-terminal cytoplasmic tail of 9 residues and a single transmembrane domain. The extracellular domain contains 3 potential N-glycosylation sites. CHST5 shares 55% amino acid sequence identity with LSST, 35.8% identity with CHST1, and 76% identity with mouse Chst5, whose cDNA Lee et al. (1999) also cloned. Recombinant CHST5 expressed in mammalian cells catalyzed the addition of sulfate to C6 of GlcNAc. Lee et al. (1999) isolated the CHST5 genomic sequence. The CHST5 gene is intronless. Northern blot analysis of a variety of normal human tissues showed a major 2.8-kb CHST5 transcript at relatively high levels in colon and small intestine and at lower levels in fetal liver. Minor transcripts of 3.5, 4, 5, and 8 kb were also found in colon and small intestine. CHST5 expression was not detected in any of the other tissues tested. CHST5, encoding an intestinal sulfotransferase, is situated close to CHST6 (OMIM Ref. No. 605294), which encodes a corneal sulfotransferase and is mutant in cases of macular corneal dystrophy (OMIM Ref. No. 217800). By radiation hybrid analysis, Akama et al. (2000) mapped the CHST5 and CHST6 genes to 16q22, between markers D16S3326 and D16S3016

[12259] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [12260] Akama, T. O.; Nishida, K.; Nakayama, J.; Watanabe, H.; Ozaki, K.; Nakamura, T.; Dota, A.; Kawasaki, S.; Inoue, Y.; Maeda, N.; Yamamoto, S.; Fujiwara, T.; Thonar, E. J.-M. A.; Shimomura, Y.; Kinoshita, S.; Tanigami, A.; Fukuda, M. N. : Macular corneal dystrophy type I and type II are caused by distinct mutations in a new sulphotransferase gene. *Nature Genet.* 26: 237-241, 2000. ; and
- [12261] Lee, J. K.; Bhakta, S.; Rosen, S. D.; Hemmerich, S. : Cloning and characterization of a mammalian N-acetylglucosamine-6-sulfotransferase that is highly restricted to intestinal tissue.
- [12262] Further studies establishing the function and utilities of CHST5 are found in John Hopkins OMIM database record ID 604817, and in cited publications numbered 10107 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM_000896) is another VGAM186 host target gene. CYP4F3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP4F3, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP4F3 BINDING SITE, designated SEQ ID:6593, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12263] Another function of VGAM186 is therefore inhibition of Cytochrome P450, Subfamily IVF, Polypeptide 3 (leukotriene B4 omega hydroxylase) (CYP4F3, Accession NM_000896), a gene which converts leukotriene B4 into the less active 20-hydroxy-leukotriene B4. Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP4F3. The function of CYP4F3 has been established by previous studies. Leukotrienes are a group of bioactive compounds that play important roles in such processes as inflammation. Kikuta et al. (1993) isolated a cDNA for the human leukotriene B4 omega-hydroxylase (LTB4H), an enzyme which catalyzes the omega-hydroxylation of leukotriene B4. Their cDNA encoded a 520-amino acid protein with a predicted molecular weight of 59,805 Da. The deduced amino acid sequence contains a cysteine in the conserved heme-binding domain near

the C-terminus, which is a characteristic feature of the cytochrome P450 superfamily; the protein shares 31 to 44% similarity with CYP4A, CYP4B (OMIM Ref. No. 124075), and CYP4C. Kikuta et al. (1993) detected transcript from the LTB₄H gene in polymorphonuclear leukocytes and leukocytes.

[12264] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12265] Kikuta, Y.; Kato, M.; Yamashita, Y.; Miyauchi, Y.; Tanaka, K.; Kamada, N.; Kusunose, M. : Human leukotriene B₄ omega-hydroxylase (CYP4F3) gene: molecular cloning and chromosomal localization. DNA Cell Biol. 17: 221-230, 1998. ; and

[12266] Kikuta, Y.; Kusunose, E.; Endo, K.; Yamamoto, S.; Sogawa, K.; Fujii-Kuriyama, Y.; Kusunose, M. : A novel form of cytochrome P-450 family 4 in human polymorphonuclear leukocytes: cDNA cl.

[12267] Further studies establishing the function and utilities of CYP4F3 are found in John Hopkins OMIM database record ID 601270, and in cited publications numbered 9856-9857 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Gamma-glutamyl Carboxylase (GGCX, Accession NM_000821) is another VGAM186 host target gene. GGCX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GGCX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGCX BINDING SITE, designated SEQ ID:6483, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12268] Another function of VGAM186 is therefore inhibition of Gamma-glutamyl Carboxylase (GGCX, Accession NM_000821). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGCX. Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM_000901) is another VGAM186 host target gene. NR3C2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NR3C2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NR3C2 BINDING SITE, designated SEQ

ID:6596, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12269] Another function of VGAM186 is therefore inhibition of Nuclear Receptor Subfamily 3, Group C, Member 2 (NR3C2, Accession NM_000901), a gene which is to increase ion and water transport and thus raise extracellular fluid volume and blood pressure and lower potassium levels. Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR3C2. The function of NR3C2 has been established by previous studies. Arriza et al. (1987) used low-stringency hybridization with human glucocorticoid receptor cDNA to isolate a new gene encoding a predicted 107-kD polypeptide. Expression studies demonstrated its ability to bind aldosterone with high affinity and to activate gene transcription in response to aldosterone, thus establishing its identity as the human mineralocorticoid receptor. This molecule also showed high affinity for glucocorticoids. They speculated that, since the circulating level of glucocorticoids is several times higher than those of aldosterone, the primary mineralocorticoid, glucocorticoid activation of the mineralocorti-

coid receptor may be functionally significant. The gene for the estrogen receptor (OMIM Ref. No. 133430) and that for the progesterone receptor (OMIM Ref. No. 607311) have also been cloned. Animal model experiments lend further support to the function of NR3C2. Berger et al. (1998) generated MLR-deficient mice by gene targeting. These mice had a normal prenatal development. During the first week of life, the MLR-deficient mice developed symptoms of pseudohypoaldosteronism. They lost weight and eventually died at approximately 10 days after birth from dehydration by renal sodium and water loss. At day 8, MLR $-/-$ mice showed hyperkalemia, hyponatremia, and a strong increase in renin, angiotensin II, and aldosterone plasma concentrations. The fractional renal Na^+ excretion was elevated more than 8-fold. The glomerular filtration rate in MLR $-/-$ mice was not different from that in controls. The effect of amiloride on renal Na^+ excretion in colonic transepithelial voltage reflected the function of amiloride-sensitive epithelial Na^+ channels.

[12270] It is appreciated that the abovementioned animal model for NR3C2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[12271] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12272] Arriza, J. L.; Weinberger, C.; Cerelli, G.; Glaser, T. M.; Handelin, B. L.; Housman, D. E.; Evans, R. M. : Cloning of human mineralocorticoid receptor complementary DNA: structural and functional kinship with the glucocorticoid receptor. Science 237: 268–275, 1987. ; and

[12273] Berger, S.; Bleich, M.; Schmid, W.; Cole, T. J.; Peters, J.; Watanabe, H.; Kriz, W.; Warth, R.; Greger, R.; Schutz, G. : Mineralocorticoid receptor knockout mice: pathophysiology of Na⁺.

[12274] Further studies establishing the function and utilities of NR3C2 are found in John Hopkins OMIM database record ID 600983, and in cited publications numbered 7886–7887, 8592–789 and 5457–5458 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chemokine (C–C motif) Receptor 6 (CCR6, Accession NM_004367) is another VGAM186 host target gene. CCR6 BINDING SITE1 and CCR6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCR6, corresponding to HOST TARGET binding sites such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR6 BINDING SITE1 and CCR6 BINDING SITE2, designated SEQ ID:10578 and SEQ ID:25372 respectively, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12275] Another function of VGAM186 is therefore inhibition of Chemokine (C-C motif) Receptor 6 (CCR6, Accession NM_004367). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR6. FLJ10656 (Accession NM_018170) is another VGAM186 host target gene. FLJ10656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10656 BINDING SITE, designated SEQ ID:19989, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12276] Another function of VGAM186 is therefore inhibition of FLJ10656 (Accession NM_018170). Accordingly, utilities of

VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10656. FLJ10751 (Accession NM_018205) is another VGAM186 host target gene. FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ10751, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10751 BINDING SITE1 and FLJ10751 BINDING SITE2, designated SEQ ID:20097 and SEQ ID:20196 respectively, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12277] Another function of VGAM186 is therefore inhibition of FLJ10751 (Accession NM_018205). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10751. FLJ12363 (Accession NM_032167) is another VGAM186 host target gene. FLJ12363 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12363, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ12363 BINDING SITE, designated SEQ ID:25871, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12278] Another function of VGAM186 is therefore inhibition of FLJ12363 (Accession NM_032167). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12363. FLJ22054 (Accession XM_170478) is another VGAM186 host target gene. FLJ22054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22054 BINDING SITE, designated SEQ ID:45319, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12279] Another function of VGAM186 is therefore inhibition of FLJ22054 (Accession XM_170478). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22054. FLJ22167 (Accession NM_024533) is another VGAM186

host target gene. FLJ22167 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22167, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22167 BINDING SITE, designated SEQ ID:23743, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12280] Another function of VGAM186 is therefore inhibition of FLJ22167 (Accession NM_024533). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22167. FLJ31455 (Accession NM_144964) is another VGAM186 host target gene. FLJ31455 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31455, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31455 BINDING SITE, designated SEQ ID:29580, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12281] Another function of VGAM186 is therefore inhibition of FLJ31455 (Accession NM_144964). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31455. HSA249128 (Accession NM_017583) is another VGAM186 host target gene. HSA249128 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSA249128, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSA249128 BINDING SITE, designated SEQ ID:19026, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12282] Another function of VGAM186 is therefore inhibition of HSA249128 (Accession NM_017583). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSA249128. KIAA0408 (Accession NM_014702) is another VGAM186 host target gene. KIAA0408 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0408, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0408 BINDING SITE, designated SEQ ID:16235, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12283] Another function of VGAM186 is therefore inhibition of KIAA0408 (Accession NM_014702). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0408. KIAA0798 (Accession NM_014650) is another VGAM186 host target gene. KIAA0798 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0798 BINDING SITE, designated SEQ ID:16071, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12284] Another function of VGAM186 is therefore inhibition of KIAA0798 (Accession NM_014650). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0798. KIAA1950 (Accession XM_166532) is another VGAM186 host target gene. KIAA1950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1950 BINDING SITE, designated SEQ ID:44494, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12285] Another function of VGAM186 is therefore inhibition of KIAA1950 (Accession XM_166532). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1950. MGC11352 (Accession XM_035941) is another VGAM186 host target gene. MGC11352 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11352 BINDING SITE, designated SEQ ID:32357, to the nucleotide sequence of VGAM186 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2897.

[12286] Another function of VGAM186 is therefore inhibition of MGC11352 (Accession XM_035941). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11352. MRPL56 (Accession NM_032857) is another VGAM186 host target gene. MRPL56 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL56, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL56 BINDING SITE, designated SEQ ID:26659, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12287] Another function of VGAM186 is therefore inhibition of MRPL56 (Accession NM_032857). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL56. Netrin 4 (NTN4, Accession XM_031896) is another VGAM186 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTN4, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTN4 BINDING SITE, designated SEQ ID:31516, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12288] Another function of VGAM186 is therefore inhibition of Netrin 4 (NTN4, Accession XM_031896). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. Ring Finger Protein 11 (RNF11, Accession NM_014372) is another VGAM186 host target gene. RNF11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF11 BINDING SITE, designated SEQ ID:15707, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12289] Another function of VGAM186 is therefore inhibition of Ring Finger Protein 11 (RNF11, Accession NM_014372).

Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF11. LOC116071 (Accession NM_138456) is another VGAM186 host target gene. LOC116071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116071 BINDING SITE, designated SEQ ID:28816, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12290] Another function of VGAM186 is therefore inhibition of LOC116071 (Accession NM_138456). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116071. LOC159036 (Accession XM_099018) is another VGAM186 host target gene. LOC159036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC159036 BINDING SITE, designated SEQ ID:42055, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12291] Another function of VGAM186 is therefore inhibition of LOC159036 (Accession XM_099018). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159036. LOC196540 (Accession XM_116933) is another VGAM186 host target gene. LOC196540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196540 BINDING SITE, designated SEQ ID:43152, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12292] Another function of VGAM186 is therefore inhibition of LOC196540 (Accession XM_116933). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196540. LOC220662 (Accession XM_165978) is an-

other VGAM186 host target gene. LOC220662 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220662, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220662 BINDING SITE, designated SEQ ID:43826, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12293] Another function of VGAM186 is therefore inhibition of LOC220662 (Accession XM_165978). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220662. LOC221178 (Accession XM_167936) is another VGAM186 host target gene. LOC221178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221178, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221178 BINDING SITE, designated SEQ ID:44929, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12294] Another function of VGAM186 is therefore inhibition of LOC221178 (Accession XM_167936). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221178. LOC221490 (Accession XM_168084) is another VGAM186 host target gene. LOC221490 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221490, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221490 BINDING SITE, designated SEQ ID:44986, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12295] Another function of VGAM186 is therefore inhibition of LOC221490 (Accession XM_168084). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221490. LOC254100 (Accession XM_172851) is another VGAM186 host target gene. LOC254100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254100, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254100 BINDING SITE, designated SEQ ID:46130, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12296] Another function of VGAM186 is therefore inhibition of LOC254100 (Accession XM_172851). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254100. LOC255328 (Accession XM_172920) is another VGAM186 host target gene. LOC255328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255328 BINDING SITE, designated SEQ ID:46181, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12297] Another function of VGAM186 is therefore inhibition of LOC255328 (Accession XM_172920). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC255328. LOC90072 (Accession XM_028702) is another VGAM186 host target gene. LOC90072 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90072, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90072 BINDING SITE, designated SEQ ID:30730, to the nucleotide sequence of VGAM186 RNA, herein designated VGAM RNA, also designated SEQ ID:2897.

[12298] Another function of VGAM186 is therefore inhibition of LOC90072 (Accession XM_028702). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90072. LOC92267 (Accession XM_043979) is another VGAM186 host target gene. LOC92267 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92267, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92267 BINDING SITE, designated SEQ ID:34060, to the nucleotide sequence of VGAM186 RNA, herein designated

VGAM RNA, also designated SEQ ID:2897.

[12299] Another function of VGAM186 is therefore inhibition of LOC92267 (Accession XM_043979). Accordingly, utilities of VGAM186 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92267. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 187 (VGAM187) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12300] VGAM187 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM187 was detected is described hereinabove with reference to Figs. 1–8.

[12301] VGAM187 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12302] VGAM187 gene encodes a VGAM187 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM187 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM187 precursor RNA is designated SEQ ID:173, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:173 is located at position 290507 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12303] VGAM187 precursor RNA folds onto itself, forming VGAM187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12304] An enzyme complex designated DICER COMPLEX, `dices` the VGAM187 folded precursor RNA into VGAM187 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM187 RNA is designated SEQ ID:2898, and is provided hereinbelow with reference to the sequence listing part.

[12305] VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM187 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12306] VGAM187 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM187 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM187 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12307] The complementary binding of VGAM187 RNA, herein designated VGAM RNA, to host target binding sites on VGAM187 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM187 host target RNA into VGAM187 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12308] It is appreciated that VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM187 host target genes. The mRNA of each one of this plurality of VGAM187 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM187 RNA, herein designated VGAM RNA, and which when bound by VGAM187 RNA causes inhibition of translation of respective one or more VGAM187 host target proteins.

[12309] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM187 gene, herein designated VGAM GENE, on one or more VGAM187 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[12310] It is yet further appreciated that a function of VGAM187 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM187 correlate with, and may be deduced from, the identity of the host target genes which VGAM187 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12311] Nucleotide sequences of the VGAM187 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM187 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM187 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM187 are further described hereinbelow with reference to Table 1.

[12312] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM187 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM187 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12313] As mentioned hereinabove with reference to Fig. 1, a function of VGAM187 gene, herein designated VGAM is inhibition of expression of VGAM187 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM187 correlate with, and may be deduced from, the identity of the target genes which VGAM187 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12314] Ankyrin 1, Erythrocytic (ANK1, Accession NM_000037) is a VGAM187 host target gene. ANK1 BINDING SITE1 through ANK1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ANK1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE1 through ANK1 BINDING SITE3, designated SEQ ID:5475, SEQ ID:21728 and SEQ ID:30278 respectively, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2898.

[12315] A function of VGAM187 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession NM_000037). Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2) (GALNT2, Accession NM_004481) is another VGAM187 host target gene. GALNT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT2 BINDING SITE, designated SEQ ID:10800, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, also designated SEQ ID:2898.

[12316] Another function of VGAM187 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2) (GALNT2, Accession NM_004481), a gene which catalyzes the initial reaction in o-linked oligosaccharide biosynthesis. Accord-

ingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT2. The function of GALNT2 has been established by previous studies. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase (GalNAc-T; EC 2.4.1.41) transfers an N-acetyl galactosamine (OMIM Ref. No. GalNAc) to the hydroxyl group of a serine or threonine residue in the first step of O-linked oligosaccharide biosynthesis. White et al. (1995) purified GALNT2, termed GalNAc-T2 by them, from human placenta, using a defined synthetic acceptor peptide as an affinity ligand. They also identified a cDNA for GALNT2 using polymerase chain reaction with primers derived from the protein sequence of the purified GALNT2. The GALNT2 cDNA encodes a predicted 571-amino acid protein of approximately 64 kD (White et al., 1995). Bennett et al. (1998) found that the GALNT1 (OMIM Ref. No. 602273), GALNT2, and GALNT3 (OMIM Ref. No. 601756) genes contain 11, 16, and 10 exons, respectively. Several intron/exon boundaries are conserved within the 3 genes. By FISH, Bennett et al. (1998) mapped the GALNT2 gene to chromosome 1q41-q42.

[12317] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12318] Bennett, E. P.; Weghuis, D. O.; Merkx, G.; Geurts van Kessel, A.; Eiberg, H.; Clausen, H. : Genomic organization and chromosomal localization of three members of the UDP-N-acetylgalactosamine:polypeptide N-acetylgalactosaminyltransferase family. *Glycobiology* 8: 547-555, 1998. ; and

[12319] White, T.; Bennett, E. P.; Takio, K.; Sorensen, T.; Bonding, N.; Clausen, H. : Purification and cDNA cloning of a human UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosam.

[12320] Further studies establishing the function and utilities of GALNT2 are found in John Hopkins OMIM database record ID 602274, and in cited publications numbered 2824 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM_130838) is another VGAM187 host target gene. UBE3A BINDING SITE1 through UBE3A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

UBE3A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE3A BINDING SITE1 through UBE3A BINDING SITE3, designated SEQ ID:28361, SEQ ID:28365 and SEQ ID:6080 respectively, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, also designated SEQ ID:2898.

[12321] Another function of VGAM187 is therefore inhibition of Ubiquitin Protein Ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome) (UBE3A, Accession NM_130838). Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE3A. Paraneoplastic Antigen MA1 (PNMA1, Accession NM_006029) is another VGAM187 host target gene. PNMA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PNMA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PNMA1 BINDING SITE, designated SEQ ID:12645, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA,

also designated SEQ ID:2898.

[12322] Another function of VGAM187 is therefore inhibition of Paraneoplastic Antigen MA1 (PNMA1, Accession NM_006029). Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PNMA1. Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM_003958) is another VGAM187 host target gene. RNF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF8 BINDING SITE, designated SEQ ID:10093, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, also designated SEQ ID:2898.

[12323] Another function of VGAM187 is therefore inhibition of Ring Finger Protein (C3HC4 type) 8 (RNF8, Accession NM_003958). Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF8. LOC256642 (Accession XM_172797) is another VGAM187 host target gene. LOC256642 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by LOC256642, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256642 BINDING SITE, designated SEQ ID:46079, to the nucleotide sequence of VGAM187 RNA, herein designated VGAM RNA, also designated SEQ ID:2898.

[12324] Another function of VGAM187 is therefore inhibition of LOC256642 (Accession XM_172797). Accordingly, utilities of VGAM187 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256642. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 188 (VGAM188) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12325] VGAM188 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM188 was detected is described hereinabove with reference to Figs. 1-8.

[12326] VGAM188 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12327] VGAM188 gene encodes a VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM188 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM188 precursor RNA is designated SEQ ID:174, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:174 is located at position 52782 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12328] VGAM188 precursor RNA folds onto itself, forming VGAM188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12329] An enzyme complex designated DICER COMPLEX, `dices` the VGAM188 folded precursor RNA into VGAM188 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM188 RNA is designated SEQ ID:2899, and is provided hereinbelow with reference to the sequence listing part.

[12330] VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM188 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12331] VGAM188 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM188 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM188 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM188 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12332] The complementary binding of VGAM188 RNA, herein designated VGAM RNA, to host target binding sites on VGAM188 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM188 host target RNA into VGAM188 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12333] It is appreciated that VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM188 host target genes. The mRNA of each one of this plurality of VGAM188 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM188 RNA, herein designated VGAM RNA, and which when bound by VGAM188 RNA causes inhibition of translation of respective one or more VGAM188 host target proteins.

[12334] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM188 gene, herein designated VGAM GENE, on one or more VGAM188 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12335] It is yet further appreciated that a function of VGAM188 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM188 correlate with, and may be deduced from, the identity of the host target genes which VGAM188 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12336] Nucleotide sequences of the VGAM188 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM188 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM188 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM188 are further described hereinbelow with reference to Table 1.

[12337] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM188 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM188 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12338] As mentioned hereinabove with reference to Fig. 1, a function of VGAM188 gene, herein designated VGAM is inhibition of expression of VGAM188 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM188 correlate with, and may be deduced from, the identity of the target genes which VGAM188 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12339] V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM_005163) is a VGAM188 host target gene. AKT1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by AKT1,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT1 BINDING SITE, designated SEQ ID:11652, to the nucleotide sequence of VGAM188 RNA, herein designated VGAM RNA, also designated SEQ ID:2899.

[12340] A function of VGAM188 is therefore inhibition of V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM_005163), a gene which Serine-threonine protein kinase. Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT1. The function of AKT1 has been established by previous studies. Phosphoinositide 3-kinases, or PI3Ks (see OMIM Ref. No. PIK3CA; 171834), generate specific inositol lipids implicated in the regulation of cell growth, proliferation, survival, differentiation, and cytoskeletal changes. One of the best characterized targets of PI3K lipid products is the protein kinase AKT, or protein kinase B (PKB). In quiescent cells, PKB resides in the cytosol in a low-activity conformation. Upon cellular stimulation, PKB is activated through recruitment to cellular membranes by PI3K lipid products and by phosphorylation by 3-prime phosphoinositide-dependent

kinase-1 (PDPK1; 605213). For a review of the mechanism that activates PKB and the downstream actions of this multifunctional kinase, see Vanhaesebroeck and Alessi (2000). For a review of the possible role of PKB in glucose transport, see Hajdуч et al. (2001). Animal model experiments lend further support to the function of AKT1. Holland et al. (2000) transferred, in a tissue-specific manner, genes encoding activated forms of Ras (OMIM Ref. No. 190070) and Akt to astrocytes and neural progenitors in mice. Holland et al. (2000) found that although neither activated Ras nor Akt alone was sufficient to induce glioblastoma multiforme (GBM; 137800) formation, the combination of activated Ras and Akt induced high-grade gliomas with the histologic features of human GBMs. These tumors appeared to arise after gene transfer to neural progenitors, but not after transfer to differentiated astrocytes. Increased activity of RAS is found in many human GBMs, and Holland et al. (2000) demonstrated that Akt activity is increased in most of these tumors, implying that combined activation of these 2 pathways accurately models the biology of this disease. By targeted disruption of the Akt1 gene, Chen et al. (2001) created an Akt1 null mouse model. Homozygous mice were viable but smaller

than wildtype littermates, and they did not display a diabetic phenotype. Upon exposure to genotoxic stress, their life span was shorter. Chen et al. (2001) found that the Akt1 null mice showed increased spontaneous apoptosis in testes and thymi. They observed an attenuation of spermatogenesis in the Akt1 null male mice, and thymocytes were more sensitive to gamma irradiation and dexamethasone-induced apoptosis. Akt1 null mouse embryo fibroblasts were also more susceptible to apoptosis induced by TNF, anti-Fas (OMIM Ref. No. 134637), ultraviolet irradiation, and serum withdrawal.

[12341] It is appreciated that the abovementioned animal model for AKT1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12342] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12343] Vanhaesebroeck, B.; Alessi, D. R. : The PI3K-PDK1 connection: more than just a road to PKB. *Biochem. J.* 346: 561-576, 2000. ; and

[12344] Hajdуч, E.; Litherland, G. J.; Hundal, H. S. : Protein kinase B (PKB/Akt)--a key regulator of glucose transport? *FEBS*

Lett. 492: 199–203, 2001.

[12345] Further studies establishing the function and utilities of AKT1 are found in John Hopkins OMIM database record ID 164730, and in cited publications numbered 11046–11049, 11203, 11215–11217, 11033, 11218–11220, 4713, 11221–11223, 1273 and 12740–11229 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Recombination Activating Gene 1 (RAG1, Accession NM_000448) is another VGAM188 host target gene. RAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAG1 BINDING SITE, designated SEQ ID:6042, to the nucleotide sequence of VGAM188 RNA, herein designated VGAM RNA, also designated SEQ ID:2899.

[12346] Another function of VGAM188 is therefore inhibition of Recombination Activating Gene 1 (RAG1, Accession NM_000448). Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAG1. FLJ10856 (Accession

NM_018247) is another VGAM188 host target gene. FLJ10856 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10856 BINDING SITE, designated SEQ ID:20218, to the nucleotide sequence of VGAM188 RNA, herein designated VGAM RNA, also designated SEQ ID:2899.

[12347] Another function of VGAM188 is therefore inhibition of FLJ10856 (Accession NM_018247). Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10856. KIAA0157 (Accession NM_032182) is another VGAM188 host target gene. KIAA0157 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0157 BINDING SITE, designated SEQ ID:25897, to the nucleotide sequence of VGAM188 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2899.

[12348] Another function of VGAM188 is therefore inhibition of KIAA0157 (Accession NM_032182). Accordingly, utilities of VGAM188 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0157. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 189 (VGAM189) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12349] VGAM189 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM189 was detected is described hereinabove with reference to Figs. 1–8.

[12350] VGAM189 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12351] VGAM189 gene encodes a VGAM189 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM189 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM189 precursor RNA is designated SEQ ID:175, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:175 is located at position 194768 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12352] VGAM189 precursor RNA folds onto itself, forming VGAM189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12353] An enzyme complex designated DICER COMPLEX, `dices` the VGAM189 folded precursor RNA into VGAM189 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM189 RNA is designated SEQ ID:2900, and is provided hereinbelow with reference to the sequence listing part.

[12354] VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM189 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12355] VGAM189 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM189 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM189 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12356] The complementary binding of VGAM189 RNA, herein designated VGAM RNA, to host target binding sites on VGAM189 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM189 host target RNA into VGAM189 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12357] It is appreciated that VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM189 host target genes. The mRNA of each one of this plurality of VGAM189 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM189 RNA, herein designated VGAM RNA, and which when bound by VGAM189 RNA causes inhibition of translation of respective one or more VGAM189 host target proteins.

[12358] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM189 gene, herein designated VGAM GENE, on one or more VGAM189 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[12359] It is yet further appreciated that a function of VGAM189 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM189 correlate with, and may be deduced from, the identity of the host target genes which VGAM189 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12360] Nucleotide sequences of the VGAM189 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM189 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM189 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM189 are further described hereinbelow with reference to Table 1.

[12361] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM189 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM189 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12362] As mentioned hereinabove with reference to Fig. 1, a function of VGAM189 gene, herein designated VGAM is inhibition of expression of VGAM189 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM189 correlate with, and may be deduced from, the identity of the target genes which VGAM189 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12363] Chromosome 14 Open Reading Frame 1 (C14orf1, Accession NM_007176) is a VGAM189 host target gene. C14orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C14orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C14orf1 BINDING SITE, designated SEQ ID:14030, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12364] A function of VGAM189 is therefore inhibition of Chromosome 14 Open Reading Frame 1 (C14orf1, Accession NM_007176). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C14orf1. Early Growth Response 3 (EGR3, Accession XM_005040) is another VGAM189 host target gene. EGR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR3 BINDING SITE, designated SEQ ID:29959, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12365] Another function of VGAM189 is therefore inhibition of Early Growth Response 3 (EGR3, Accession XM_005040), a gene which is a putative transcription factor. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR3. The function of EGR3 has been established by previous studies. The human EGR3 gene was described by Patwardhan et al. (1991) as predicting a 387-amino acid

protein containing 3 C2H2 zinc fingers nearly identical to those of EGR1 and EGR2. The EGR3 gene has a single intron. The gene was known to be induced in various brain regions in response to stress or following focal brain injury. Morris et al. (1998) stated that, in the SCN, it probably participates in the transcriptional regulation of genes in response to retinal input, as had been proposed for FOS. Muscle spindles are skeletal muscle sensory organs that provide axial and limb position information (proprioception) to the central nervous system. Spindles consist of encapsulated muscle fibers (intrafusal fibers) that are innervated by specialized motor and sensory axons. Tourtellotte and Milbrandt (1998) found that mice rendered deficient in *Egr3* by gene targeting had gait ataxia, increased frequency of perinatal mortality, scoliosis, resting tremors, and ptosis. Although extrafusal skeletal muscle fibers appeared normal, *Egr3*-deficient animals lacked muscle spindles, a finding that is consistent with their profound gait ataxia. *Egr3* was highly expressed in developing muscle spindles, but not in Ia afferent neurons or their terminals during developmental periods that coincided with the induction of spindle morphogenesis by sensory afferent axons. These results indi-

cated that type I myotubes are dependent upon Egr3-mediated transcription for proper spindle development.

[12366] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12367] Morris, M. E.; Viswanathan, N.; Kuhlman, S.; Davis, F. C.; Weitz, C. J. : A screen for genes induced in the suprachiasmatic nucleus by light. *Science* 279: 1544–1547, 1998.
; and

[12368] Tourtellotte, W. G.; Milbrandt, J. : Sensory ataxia and muscle spindle agenesis in mice lacking the transcription factor Egr3. *Nature Genet.* 20: 87–91, 1998.

[12369] Further studies establishing the function and utilities of EGR3 are found in John Hopkins OMIM database record ID 602419, and in cited publications numbered 1029–1031 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hyaluronoglucosaminidase 4 (HYAL4, Accession NM_012269) is another VGAM189 host target gene. HYAL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HYAL4, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HYAL4 BINDING SITE, designated SEQ ID:14593, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12370] Another function of VGAM189 is therefore inhibition of Hyaluronoglucosaminidase 4 (HYAL4, Accession NM_012269). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HYAL4. Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha (PKIA, Accession NM_006823) is another VGAM189 host target gene. PKIA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PKIA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKIA BINDING SITE, designated SEQ ID:13695, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12371] Another function of VGAM189 is therefore inhibition of Protein Kinase (cAMP-dependent, catalytic) Inhibitor Alpha

(PKIA, Accession NM_006823). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKIA. POU Domain, Class 2, Associating Factor 1 (POU2AF1, Accession NM_006235) is another VGAM189 host target gene. POU2AF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU2AF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU2AF1 BINDING SITE, designated SEQ ID:12889, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12372] Another function of VGAM189 is therefore inhibition of POU Domain, Class 2, Associating Factor 1 (POU2AF1, Accession NM_006235), a gene which is a transcriptional coactivator that specifically associates with either oct1 or oct2. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU2AF1. The function of POU2AF1 and its association with various diseases and clinical conditions, has been established by previous studies, as de-

scribed hereinabove with reference to VGAM171.Telomeric Repeat Binding Factor (NIMA-interacting) 1 (TERF1, Accession NM_017489) is another VGAM189 host target gene. TERF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TERF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TERF1 BINDING SITE, designated SEQ ID:18952, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12373] Another function of VGAM189 is therefore inhibition of Telomeric Repeat Binding Factor (NIMA-interacting) 1 (TERF1, Accession NM_017489), a gene which negatively regulates telomere length, involves in regulation of the mitotic spindle. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TERF1. The function of TERF1 has been established by previous studies. Human chromosomes carry at their termini long arrays of double-stranded hexamers (OMIM Ref. No. TTAGGG) that are maintained by the enzyme telomerase (OMIM Ref. No.

187270). Chong et al. (1995) noted that telomeric DNA is thought to form a protective nucleoprotein cap through its association with telomere-specific proteins; also see review by Zakian (1995). Because the loss of telomere function can induce cell cycle arrest and genome instability, the telomeric complex is probably required in all human cells. Changes in the structure and function of human telomeres are thought to play a role in malignant transformation and cellular senescence. Protein components of the telomeric complex had been identified in ciliates and yeast, but not in vertebrate systems. Quests for vertebrate telomeric proteins had yielded a single candidate that could potentially bind along the length of the telomeric TTAGGG repeat array. This protein, called TRF (telomeric repeat-binding factor) by Chong et al. (1995), was shown by the authors to associate with double-stranded TTAGGG repeat arrays in vitro. TRF displays strong specificity for vertebrate telomere DNA. Human TRF activity is detectable in HeLa cell nuclear extracts on the basis of its ability to alter the mobility of double-stranded DNA fragments containing the sequence (OMIM Ref. No. TTAGGG)¹². Using this assay, Chong et al. (1995) purified HeLa TRF to near homogeneity. Three independent preparations of purified

TRF contained a protein in the 60–kD apparent molecular mass range, which copurified with TRF activity over a column containing double-stranded TTAGGG repeats. Amino acid sequences revealed sequence identity to an anonymous partial cDNA in the GenBank database. On the basis of this nucleotide sequence, cDNAs were isolated from a HeLa cell library, sequenced, and found to contain an open reading frame encoding all sequence peptides. The cDNA hybridized 2 mRNAs of approximately 1.8 and 3.0 kb that are expressed in a variety of human tissues. The cDNA derived from the larger mRNA revealed an open reading frame encoding a 439–amino acid protein. In vitro transcription and translation of the cloned cDNA produced a protein of the same size as purified HeLa TRF. Comparison with the sequence information in the databases indicated that human TRF is a novel protein with 3 previously recognized sequence motifs. There is one DNA-binding repeat resembling that of MYB (OMIM Ref. No. 189990) and an N-terminal acidic domain. Immunofluorescent labeling showed that TRF specifically colocalizes with telomeric DNA in human metaphase cells and is located at chromosome ends during metaphase. Chong et al. (1995) stated that the presence of TRF along the telomeric

TTAGGG repeat array demonstrates that human telomeres form a specialized nuclear protein complex. In yeast, Marcand et al. (1997) demonstrated a protein-counting mechanism for regulation of the length of telomeres. This mechanism involves the telomere repeat-binding protein Rap1p. Because the structural and functional properties of telomeres appear to be highly conserved, Marcand et al. (1997) suggested that their findings may be relevant to telomere length regulation in humans, which has been associated with aging and cancer. Okabe et al. (2000) investigated cellular factors required for telomere formation using the frequency of telomere seeding as an index and identified TRF1 as an essential transacting factor. The exogenous telomere repeat induced telomere formation at a frequency determined by the availability of TRF1, even in telomerase-negative cells. The authors concluded that TRF1 has a novel physiologic significance distinct from its role as a regulator of telomere length in the endogenous chromosome.

[12374] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12375] Chong, L.; van Steensel, B.; Broccoli, D.; Erdjument-Bro-

- mage, H.; Hanish, J.; Tempst, P.; de Lange, T. : A human telomeric protein. *Science* 270: 1663–1667, 1995. ; and
- [12376] Okabe, J.; Eguchi, A.; Masago, A.; Hayakawa, T.; Nakanishi, M. : TRF1 is a critical trans-acting factor required for de novo telomere formation in human cells. *Hum. Molec. Genet.* 9: 263.
- [12377] Further studies establishing the function and utilities of TERF1 are found in John Hopkins OMIM database record ID 600951, and in cited publications numbered 9620–9628 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TIRAP (Accession NM_052887) is another VGAM189 host target gene. TIRAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIRAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIRAP BINDING SITE, designated SEQ ID:27476, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.
- [12378] Another function of VGAM189 is therefore inhibition of TIRAP (Accession NM_052887), a gene which is a adapter involved in the TLR4 signaling pathway in the innate im-

mune response. Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIRAP. The function of TIRAP has been established by previous studies. Different Toll-like receptors (e.g., TLR5, 603031) are part of the innate immune system and recognize pathogen-associated molecular patterns (PAMPs). TLR4 recognizes the lipopolysaccharide of gram-negative bacteria and, like other TLRs, signals through a Toll/IL1R (OMIM Ref. No. 147810) (TIR) domain. MYD88 (OMIM Ref. No. 602170) is an adaptor protein containing a TIR domain and is involved in TLR2 (OMIM Ref. No. 603028), TLR4, TLR5, and TLR9 (OMIM Ref. No. 605474) signaling. By high-throughput sequencing of a dendritic cell EST cDNA library followed by PCR, Fitzgerald et al. (2001) identified a cDNA encoding a MYD88-adaptor-like protein, which they termed MAL. Sequence analysis predicted that the cytoplasmic protein contains a C-terminal TIR domain expected to have a secondary structure similar to that of TLR2 and an N-terminal region lacking a death domain and that is shorter than that of MYD88. Northern blot analysis revealed wide expression of a 2.3-kb transcript, with particularly strong expression in kidney, liver, heart,

and placenta. RT-PCR analysis detected expression in murine dendritic and murine and human monocyte/macrophage cell lines. Using mutational and functional analyses, Horng et al. (2001) determined that TIRAP functions downstream of TLR4, but not IL1R or TLR9.

Lipopolysaccharide or CpG stimulation results in PRKR (OMIM Ref. No. 176871) phosphorylation, indicating that PRKR is a component of both the TLR4 and TLR9 pathways. Immunoprecipitation analysis showed that PRKR, as well as its activator PACT (PRKRA; 603424) and inhibitor p58 (DNAJC3; 601184), are associated with TIRAP. Treatment of a macrophage cell line with an N-terminal mouse Tirap peptide containing the proline-125 region linked to the C terminus of 'antennapedia,' a *Drosophila* transcription factor, potently inhibited lipopolysaccharide-induced, but not CpG-induced or IL1 β -induced, NF κ B or JNK activation, suggesting a potential antiinflammatory molecule. Likewise, the Tirap peptide inhibited CD80 (OMIM Ref. No. 112203) and CD86 (OMIM Ref. No. 601020) upregulation as well as IL12 (OMIM Ref. No. 161560) and IL6 (OMIM Ref. No. 147620) cytokine production in lipopolysaccharide-activated dendritic cells. Horng et al. (2001) concluded that TIRAP functions downstream of TLR4, but not

TLR9, TLR2, or IL1R, and upstream of PRKR, probably in the TLR4/MYD88-independent pathway.

[12379] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12380] Fitzgerald, K. A.; Palsson-McDermott, E. M.; Bowie, A. G.; Jefferies, C. A.; Mansell, A. S.; Brady, G.; Brint, E.; Dunne, A.; Gray, P.; Harte, M. T.; McMurray, D.; Smith, D. E.; Sims, J. E.; Bird, T. A.; O'Neill, L. A. J. : Mal (MyD88-adaptor-like) is required for Toll-like receptor-4 signal transduction. Nature 413: 78-83, 2001. ; and

[12381] Horng, T.; Barton, G. M.; Medzhitov, R. : TIRAP: an adapter molecule in the Toll signaling pathway. Nature Immun. 2: 835-841, 2001.

[12382] Further studies establishing the function and utilities of TIRAP are found in John Hopkins OMIM database record ID 606252, and in cited publications numbered 6137-6138 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Baculoviral IAP Repeat-containing 3 (BIRC3, Accession XM_040715) is another VGAM189 host target gene. BIRC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BIRC3, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC3 BINDING SITE, designated SEQ ID:33370, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12383] Another function of VGAM189 is therefore inhibition of Baculoviral IAP Repeat-containing 3 (BIRC3, Accession XM_040715). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC3. Dynein, Axonemal, Light Polypeptide 4 (DNAL4, Accession NM_005740) is another VGAM189 host target gene. DNAL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAL4 BINDING SITE, designated SEQ ID:12304, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12384] Another function of VGAM189 is therefore inhibition of Dynein, Axonemal, Light Polypeptide 4 (DNAL4, Accession

NM_005740). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAL4. FLJ10656 (Accession NM_018170) is another VGAM189 host target gene. FLJ10656 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10656, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10656 BINDING SITE, designated SEQ ID:19987, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12385] Another function of VGAM189 is therefore inhibition of FLJ10656 (Accession NM_018170). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10656. FLJ21240 (Accession NM_024847) is another VGAM189 host target gene. FLJ21240 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ21240 BINDING SITE, designated SEQ ID:24280, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12386] Another function of VGAM189 is therefore inhibition of FLJ21240 (Accession NM_024847). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21240. FLJ21302 (Accession NM_022901) is another VGAM189 host target gene. FLJ21302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21302 BINDING SITE, designated SEQ ID:23184, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12387] Another function of VGAM189 is therefore inhibition of FLJ21302 (Accession NM_022901). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21302. KIAA0931 (Accession XM_041191) is another VGAM189

host target gene. KIAA0931 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0931, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0931 BINDING SITE, designated SEQ ID:33484, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12388] Another function of VGAM189 is therefore inhibition of KIAA0931 (Accession XM_041191). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0931. KIAA1348 (Accession XM_043826) is another VGAM189 host target gene. KIAA1348 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1348 BINDING SITE, designated SEQ ID:34028, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12389] Another function of VGAM189 is therefore inhibition of KIAA1348 (Accession XM_043826). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1348. Nucleoredoxin (NXN, Accession NM_022463) is another VGAM189 host target gene. NXN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NXN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NXN BINDING SITE, designated SEQ ID:22804, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12390] Another function of VGAM189 is therefore inhibition of Nucleoredoxin (NXN, Accession NM_022463). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NXN. LOC147299 (Accession XM_085763) is another VGAM189 host target gene. LOC147299 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147299, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147299 BINDING SITE, designated SEQ ID:38334, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12391] Another function of VGAM189 is therefore inhibition of LOC147299 (Accession XM_085763). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147299. LOC152627 (Accession XM_087495) is another VGAM189 host target gene. LOC152627 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39293, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12392] Another function of VGAM189 is therefore inhibition of LOC152627 (Accession XM_087495). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC152627. LOC221395 (Accession XM_166354) is another VGAM189 host target gene. LOC221395 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221395, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221395 BINDING SITE, designated SEQ ID:44183, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12393] Another function of VGAM189 is therefore inhibition of LOC221395 (Accession XM_166354). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221395. LOC222001 (Accession XM_167489) is another VGAM189 host target gene. LOC222001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222001 BINDING SITE, designated SEQ ID:44640, to the nucleotide sequence of VGAM189 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2900.

[12394] Another function of VGAM189 is therefore inhibition of LOC222001 (Accession XM_167489). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222001. LOC222070 (Accession XM_168433) is another VGAM189 host target gene. LOC222070 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222070 BINDING SITE, designated SEQ ID:45174, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12395] Another function of VGAM189 is therefore inhibition of LOC222070 (Accession XM_168433). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222070. LOC255326 (Accession XM_172832) is another VGAM189 host target gene. LOC255326 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255326, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255326 BINDING SITE, designated SEQ ID:46105, to the nucleotide sequence of VGAM189 RNA, herein designated VGAM RNA, also designated SEQ ID:2900.

[12396] Another function of VGAM189 is therefore inhibition of LOC255326 (Accession XM_172832). Accordingly, utilities of VGAM189 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255326. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 190 (VGAM190) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12397] VGAM190 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM190 was detected is described hereinabove with reference to Figs. 1–8.

[12398] VGAM190 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syn–

drome Virus (white spot bacilliform virus). VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12399] VGAM190 gene encodes a VGAM190 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM190 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM190 precursor RNA is designated SEQ ID:176, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:176 is located at position 18488 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12400] VGAM190 precursor RNA folds onto itself, forming VGAM190 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12401] An enzyme complex designated DICER COMPLEX, `dices` the VGAM190 folded precursor RNA into VGAM190 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM190 RNA is designated SEQ ID:2901, and is provided hereinbelow with reference to the sequence listing part.

[12402] VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM190 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12403] VGAM190 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM190 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM190 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12404] The complementary binding of VGAM190 RNA, herein designated VGAM RNA, to host target binding sites on VGAM190 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM190 host tar-

get RNA into VGAM190 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12405] It is appreciated that VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM190 host target genes. The mRNA of each one of this plurality of VGAM190 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM190 RNA, herein designated VGAM RNA, and which when bound by VGAM190 RNA causes inhibition of translation of respective one or more VGAM190 host target proteins.

[12406] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM190 gene, herein designated VGAM GENE, on one or more VGAM190 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12407] It is yet further appreciated that a function of VGAM190 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM190 correlate with, and may be deduced from, the identity of the host target genes which VGAM190 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12408] Nucleotide sequences of the VGAM190 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM190 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM190 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM190 are further described hereinbelow with reference to Table 1.

[12409] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM190 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM190 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12410] As mentioned hereinabove with reference to Fig. 1, a function of VGAM190 gene, herein designated VGAM is inhibition of expression of VGAM190 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM190 correlate with, and may be deduced from, the identity of the target genes which VGAM190 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12411] B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A, Accession NM_022893) is a VGAM190 host target gene. BCL11A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of BCL11A BINDING SITE, designated SEQ ID:23152, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12412] A function of VGAM190 is therefore inhibition of B-cell CLL/lymphoma 11A (zinc finger protein) (BCL11A, Accession NM_022893), a gene which acts as a transcriptional repressor. Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11A. The function of BCL11A has been established by previous studies. By screening a fetal brain cDNA library with mouse Evi9 as probe, Saiki et al. (2000) isolated a cDNA encoding EVI9, also termed BCL11A, and a shorter splice variant, EVI9C. Sequence analysis predicted that the 797-amino acid BCL11A protein, which is 99% identical to the mouse protein apart from an additional 35 N-terminal residues, contains 3 C2H2-type zinc finger motifs, a proline-rich region, and an acidic domain. Northern blot analysis revealed highest expression in brain, spleen, and testis. RT-PCR analysis detected expression in most hematopoietic cells but downregulation during monocytic differentiation.

Satterwhite et al. (2001) reported the recurrent involvement and deregulated expression of BCL11A in 4 cases of B-cell malignancy with the translocation t(2;14)(p13;q32.3). They noted that this translocation is a rare cytogenetic abnormality in the clinically aggressive subset of B-cell chronic lymphocytic leukemia (OMIM Ref. No. 151400)/immunocytoma. FISH analysis showed colocalization of BCL11A and REL (OMIM Ref. No. 164910) in B-cell non-Hodgkin lymphoma (OMIM Ref. No. 605027). Satterwhite et al. (2001) also identified a BCL11A homolog, BCL11B (OMIM Ref. No. 606558). Comparative genomic hybridization studies showed gains in chromosome region 2p as the most common imbalance in classical Hodgkin lymphoma. The minimal region of gain contained 2 candidate oncogenes, REL and BCL11A. Martin-Subero et al. (2002) examined the involvement of REL and BCL11A loci in 44 primary cases of classic Hodgkin lymphoma by combined immunophenotyping and interphase cytogenetics. A median 2p13 copy number above the tetraploid range was detected in 24 (55%) cases. One case displayed selective amplification of the REL locus not affecting BCL11A. Two other cases showed evidence of breakpoints in the region spanned by the REL probe.

These data indicated that REL rather than BCL11A may be the target of the 2p13 alterations in classic Hodgkin lymphoma.

[12413] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12414] Satterwhite, E.; Sonoki, T.; Willis, T. G.; Harder, L.; Nowak, R.; Arriola, E. L.; Liu, H.; Price, H. P.; Gesk, S.; Steinemann, D.; Schlegelberger, B.; Oscier, D. G.; Siebert, R.; Tucker, P. W.; Dyer, M. J. S. : The BCL11 gene family: involvement of BCL11A in lymphoid malignancies. Blood 98: 3413–3420, 2001. ; and

[12415] Martin-Subero, J. I.; Gesk, S.; Harder, L.; Sonoki, T.; Tucker, P. W.; Schlegelberger, B.; Grote, W.; Novo, F. J.; Calasanz, M. J.; Hansmann, M. L.; Dyer, M. J. S.; Siebert, R. : Recurr.

[12416] Further studies establishing the function and utilities of BCL11A are found in John Hopkins OMIM database record ID 606557, and in cited publications numbered 11660–5556 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDT6 (Accession NM_021146) is another VGAM190 host target gene. CDT6 BINDING SITE is HOST TARGET

binding site found in the 3` untranslated region of mRNA encoded by CDT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDT6 BINDING SITE, designated SEQ ID:22120, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12417] Another function of VGAM190 is therefore inhibition of CDT6 (Accession NM_021146). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDT6. GFR (Accession NM_012294) is another VGAM190 host target gene. GFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14634, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12418] Another function of VGAM190 is therefore inhibition of

GFR (Accession NM_012294). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. Hemogen (HEMGN, Accession NM_018437) is another VGAM190 host target gene. HEMGN BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HEMGN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEMGN BINDING SITE, designated SEQ ID:20499, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12419] Another function of VGAM190 is therefore inhibition of Hemogen (HEMGN, Accession NM_018437). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEMGN. KIAA0155 (Accession NM_014633) is another VGAM190 host target gene. KIAA0155 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0155 BINDING SITE, designated SEQ ID:16001, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12420] Another function of VGAM190 is therefore inhibition of KIAA0155 (Accession NM_014633). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0155. Ubiquitin Specific Protease 25 (USP25, Accession NM_013396) is another VGAM190 host target gene. USP25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP25 BINDING SITE, designated SEQ ID:15048, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12421] Another function of VGAM190 is therefore inhibition of Ubiquitin Specific Protease 25 (USP25, Accession NM_013396). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with USP25. LOC200269 (Accession XM_114175) is another VGAM190 host target gene. LOC200269 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200269, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200269 BINDING SITE, designated SEQ ID:42762, to the nucleotide sequence of VGAM190 RNA, herein designated VGAM RNA, also designated SEQ ID:2901.

[12422] Another function of VGAM190 is therefore inhibition of LOC200269 (Accession XM_114175). Accordingly, utilities of VGAM190 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200269. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 191 (VGAM191) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12423] VGAM191 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM191 was detected is described hereinabove with reference to Figs. 1–8.

[12424] VGAM191 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12425] VGAM191 gene encodes a VGAM191 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM191 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM191 precursor RNA is designated SEQ ID:177, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:177 is located at position 229393 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12426] VGAM191 precursor RNA folds onto itself, forming VGAM191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12427] An enzyme complex designated DICER COMPLEX, `dices` the VGAM191 folded precursor RNA into VGAM191 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM191 RNA is designated SEQ ID:2902, and is provided hereinbelow with reference to the sequence listing part.

[12428] VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM191 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[12429] VGAM191 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM191 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM191 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12430] The complementary binding of VGAM191 RNA, herein designated VGAM RNA, to host target binding sites on VGAM191 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM191 host target RNA into VGAM191 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12431] It is appreciated that VGAM191 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM191 host target genes. The mRNA of each one of this plurality of VGAM191 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM191 RNA, herein designated VGAM RNA, and which when bound by VGAM191 RNA causes inhibition of translation of respective one or more VGAM191 host target proteins.

[12432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM191 gene, herein designated VGAM GENE, on one or more VGAM191 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12433] It is yet further appreciated that a function of VGAM191 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM191 correlate with, and may be deduced from, the identity of the host target genes which VGAM191 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [12434] Nucleotide sequences of the VGAM191 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM191 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM191 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM191 are further described hereinbelow with reference to Table 1.
- [12435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM191 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM191 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [12436] As mentioned hereinabove with reference to Fig. 1, a function of VGAM191 gene, herein designated VGAM is inhibition of expression of VGAM191 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM191 correlate with, and may be deduced from, the identity of the target genes which VGAM191 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [12437] Chediak-Higashi Syndrome 1 (CHS1, Accession

NM_000081) is a VGAM191 host target gene. CHS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHS1 BINDING SITE, designated SEQ ID:5525, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12438] A function of VGAM191 is therefore inhibition of Chediak-Higashi Syndrome 1 (CHS1, Accession NM_000081), a gene which may sort endosomal resident proteins into late multivesicular endosome. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHS1. The function of CHS1 has been established by previous studies. Barbosa et al. (1997) identified novel mutations within the region of the coding domain common to both CHS1 isoforms in 3 CHS patients: C-to-T transitions that generated stop codons (R50X; 606897.0006 and Q1029X; 606897.0007) were found in 2 patients, and a novel frameshift mutation (deletion of nucleotides 3073 and 3074 of the coding domain) was found in a third. North-

ern blots of lymphoblastoid mRNA from CHS patients revealed loss of the largest transcript (approximately 13.5 kb) in 2 of 7 CHS patients, while the small mRNA was undiminished in abundance. These results suggested that the small isoform alone cannot complement Chediak–Higashi syndrome. All beige and CHS1 mutations that had been identified were predicted to result in either truncated or absent proteins. Although Perou et al. (1996) and Barbosa et al. (1996) reported identification of the 'beige' gene, the 2 cDNAs were quite different. Nagle et al. (1996) described the sequence of a human cDNA homologous to mouse 'beige,' identified pathologic mutations in patients with Chediak–Higashi syndrome, and clarified the discrepancies of the previous reports of sequence. Analysis of the CHS1 polypeptide demonstrated that its modular architecture is similar to that of the yeast vacuolar sorting protein VPS15. Nagle et al. (1996) screened human cDNA libraries with mouse 'beige' probes to yield the human 'beige' cDNA homolog, and found 87.9% amino acid identity between the 2 sequences. The predicted human protein comprises 3,801 amino acids, with a molecular mass of approximately 43 kD. Barbosa et al. (1997) reported the sequences of 2 major mRNA isoforms of the CHS1

gene in human and mouse. These isoforms differ both in size and in sequence at the 3-prime end of their coding domains, with a small isoform (approximately 5.8 kb) arising from incomplete splicing and reading through an intron. These mRNAs also differ in tissue distribution of transcription and in predicted biologic properties.

[12439] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12440] Karim, M. A.; Nagle, D. L.; Kandil, H. H.; Burger, J.; Moore, K. J.; Spritz, R. A. : Mutations in the Chediak–Higashi syndrome gene (CHS1) indicate requirement for the complete 3801 amino acid CHS protein. Hum. Molec. Genet. 6: 1087–1089, 1997. ; and

[12441] Barbosa, M. D. F. S.; Barrat, F. J.; Tchernev, V. T.; Nguyen, Q. A.; Mishra, V. S.; Colman, S. D.; Pastural, E.; Dufourcq-Lagelouse, R.; Fischer, A.; Holcombe, R. F.; Wallace, M. R.; Bra.

[12442] Further studies establishing the function and utilities of CHS1 are found in John Hopkins OMIM database record ID 606897, and in cited publications numbered 10101, 10102–10104, 5267–5268, 4584, 5269, 10105–1010 and 5270–5271 listed in the bibliography section hereinbelow,

which are also hereby incorporated by reference. E1A Binding Protein P300 (EP300, Accession NM_001429) is another VGAM191 host target gene. EP300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EP300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EP300 BINDING SITE, designated SEQ ID:7153, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12443] Another function of VGAM191 is therefore inhibition of E1A Binding Protein P300 (EP300, Accession NM_001429), a gene which may have a function in cell cycle regulation. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EP300. The function of EP300 has been established by previous studies. The growth-controlling functions of the adenovirus E1A oncoprotein depend on its ability to interact with a set of cellular proteins. Among these are the retinoblastoma protein, p107, p130, and p300. Eckner et al. (1994) isolated a cDNA encoding full-length human p300. p300 contains 3 cysteine- and histi-

dine-rich regions of which the most carboxy-terminal region interacts specifically with E1A. In its center, p300 contains a bromodomain, a hallmark of certain transcriptional coactivators. p300 and CREB-binding protein (CREBBP, or CBP; 600140) are highly related in primary structure (Arany et al., 1994). Several protein motifs such as a bromodomain, a KIX domain, and 3 regions rich in cys/his residues are well conserved between these 2 proteins. Animal model experiments lend further support to the function of EP300. The EP300 protein is a histone acetyltransferase that regulates transcription via chromatin remodeling and is important in the processes of cell proliferation and differentiation. A role for EP300 in cancer had been implied by the fact that it is targeted by viral oncoproteins (Arany et al., 1995), it is fused to MLL (OMIM Ref. No. 159555) in leukemia (Ida et al., 1997), and 2 missense sequence alterations in EP300 were identified in epithelial malignancies (Muraoka et al., 1996). Gayther et al. (2000) described EP300 mutations that predicted a truncated protein in 6 (3%) of 193 epithelial cancers analyzed. Of these 6 mutations, 2 were in primary tumors (a colorectal cancer and a breast cancer) and 4 were in cancer cell lines (colorectal, breast, and pancreatic). In addi-

tion, they identified a somatic in-frame insertion in a primary breast cancer and missense alterations in a primary colorectal cancer and 2 cell lines (breast and pancreatic). Inactivation of the second allele was demonstrated in 5 of the 6 cases with truncating mutations and in 2 other cases. The data showed that EP300 is mutated in epithelial cancers and provided the first evidence that it behaves as a classic tumor suppressor gene.

[12444] It is appreciated that the abovementioned animal model for EP300 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12445] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12446] Tini, M.; Benecke, A.; Um, S.-J.; Torchia, J.; Evans, R. M.; Chambon, P. : Association of CBP/p300 acetylase and thymine DNA glycosylase links DNA repair and transcription. *Molec. Cell* 9: 265–277, 2002. ; and

[12447] Lin, C. H.; Hare, B. J.; Wagner, G.; Harrison, S. C.; Maniatis, T.; Fraenkel, E. : A small domain of CBP/p300 binds diverse proteins: solution structure and functional studies. *Molec. C.*

[12448] Further studies establishing the function and utilities of EP300 are found in John Hopkins OMIM database record ID 602700, and in cited publications numbered 7969, 10673, 1792, 7102, 10674, 3381, 10686–1068 and 1045 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. GA Binding Protein Transcription Factor, Beta Subunit 1, 53kDa (GABPB1, Accession NM_005254) is another VGAM191 host target gene. GABPB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GABPB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABPB1 BINDING SITE, designated SEQ ID:11760, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12449] Another function of VGAM191 is therefore inhibition of GA Binding Protein Transcription Factor, Beta Subunit 1, 53kDa (GABPB1, Accession NM_005254), a gene which activates adenovirus E4 gene transcription. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with GABPB1. The function of GABPB1 has been established by previous studies. The GA-binding protein transcription factor, also called nuclear respiratory factor-2 (NRF2), was originally identified through its role in the expression of the adenovirus E4 gene. The GABP complex contributes to the transcriptional regulation of a number of subunits of mitochondrial enzymes, including cytochrome c oxidase (CO; OMIM Ref. No. 516030).

[12450] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12451] Gugneja, S.; Virbasius, J. V.; Scarpulla, R. C. : Four structurally distinct, non-DNA-binding subunits of human nuclear respiratory factor 2 share a conserved transcriptional activation domain. *Molec. Cell. Biol.* 15: 102-111, 1995. ; and

[12452] Sawada, J.; Goto, M.; Watanabe, H.; Handa, H.; Yoshida, M. C. : Regional mapping of two subunits of transcription factor E4TF1 to human chromosome. *Jpn. J. Cancer Res.* 86: 10-12, 1995.

[12453] Further studies establishing the function and utilities of GABPB1 are found in John Hopkins OMIM database record ID 600610, and in cited publications numbered 10057,

1005 and 10061 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Low Density Lipoprotein Receptor–related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM_004631) is another VGAM191 host target gene. LRP8 BINDING SITE1 and LRP8 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LRP8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP8 BINDING SITE1 and LRP8 BINDING SITE2, designated SEQ ID:11004 and SEQ ID:27128 respectively, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12454] Another function of VGAM191 is therefore inhibition of Low Density Lipoprotein Receptor–related Protein 8, Apolipoprotein E Receptor (LRP8, Accession NM_004631), a gene which binds vldl and transports it into cells by endocytosis. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP8. The function of LRP8 has been established by previous studies. Apolipoprotein E (APOE; 107741) is a 34–kD lipophilic protein that medi–

ates high-affinity binding of APOE-containing lipoproteins to the low density lipoprotein receptor (see OMIM Ref. No. LDLR; 606945) and the very low density lipoprotein receptor (VLDLR; 192977). By screening a human placenta cDNA library with degenerate oligonucleotides based on a highly conserved region between LDLR and VLDLR, Kim et al. (1996) identified a cDNA encoding APOE receptor-2 (OMIM Ref. No. APOER2). The predicted 963-amino acid protein contains a putative 41-amino acid signal sequence and 5 functional domains that resemble those of LDLR and VLDLR. APOER2 appears specific for APOE-containing ligands: LDLR-deficient mammalian cells expressing APOER bound APOE-rich beta-VLDL with high affinity, but bound LDL and VLDL with much lower affinities. Northern blot analysis revealed that APOER2 is expressed as 4.5- and 8.5-kb mRNAs in brain and placenta Kim et al. (1997) reported that the APOER2 gene contains 19 exons and spans approximately 60 kb. Alternative splicing generates multiple transcripts encoding receptors with different numbers of cysteine-rich repeats in the ligand-binding domain

[12455] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [12456] Kim, D.-H.; Iijima, H.; Goto, K.; Sakai, J.; Ishii, H.; Kim, H.-J.; Suzuki, H.; Kondo, H.; Saeki, S.; Yamamoto, T. : Human apolipoprotein E receptor 2: a novel lipoprotein receptor of the low density lipoprotein receptor family predominantly expressed in brain. J. Biol. Chem. 271: 8373-8380, 1996. ; and
- [12457] Kim, D.-H.; Magoori, K.; Inoue, T. R.; Mao, C. C.; Kim, H.-J.; Suzuki, H.; Fujita, T.; Endo, Y.; Saeki, S.; Yamamoto, T. T. : Exon/intron organization, chromosome localization, alternativ.
- [12458] Further studies establishing the function and utilities of LRP8 are found in John Hopkins OMIM database record ID 602600, and in cited publications numbered 10019-825 and 10024 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neurexin 1 (NRXN1, Accession NM_004801) is another VGAM191 host target gene. NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by NRXN1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

NRXN1 BINDING SITE1 and NRXN1 BINDING SITE2, designated SEQ ID:11223 and SEQ ID:28997 respectively, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12459] Another function of VGAM191 is therefore inhibition of Neurexin 1 (NRXN1, Accession NM_004801), a gene which may be involved in cell recognition, cell adhesion, and mediate intracellular signaling. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRXN1. The function of NRXN1 has been established by previous studies. Neurexins are polymorphic cell surface proteins that are expressed in neurons. They were discovered by Ushkaryov et al. (1992) in the course of cloning the presynaptic receptor for alpha-latrotoxin. Three neurexin genes, designated 1 (NRXN1), 2 (NRXN2; 600566), and 3 (NRXN3; 600567), were identified in a rat brain cDNA library by Ushkaryov et al. (1992). Ichtchenko et al. (1995) observed that each neurexin gene has 2 independent promoters which generate 2 classes of mRNAs: the longer mRNAs encode alpha-neurexins and the shorter mRNAs encode beta-neurexins. Thus, 6 principal neurexin isoforms, called neurexins I-alpha to III-beta, result, of

which neurexin I-alpha corresponds to the high molecular weight component of the alpha-latrotoxin receptor.

Ushkaryov et al. (1992) showed that rat neurexins are expressed at significant levels only in brain. Ullrich et al. (1995) found that the 6 rat neurexin isoforms are coexpressed in neurons and are distributed differentially in various brain regions. Neurexins display a remarkable evolutionarily conserved pattern of extensive alternative splicing. As a result, the total number of neurexins in brain probably exceeds 2,000 (Ullrich et al., 1995).

Neurexins contain epidermal growth factor-like sequences and domains homologous to the G domain repeats of laminin A (LAMA; 150320), indicating a function in cell-cell interactions. Animal model experiments lend further support to the function of NRXN1. Alpha-latrotoxin is a potent neurotoxin from black widow spider venom that binds to presynaptic receptors and causes massive neurotransmitter release. In rat, 2 alpha-latrotoxin receptors have been identified: neurexin I-alpha, which binds the toxin in a calcium-dependent manner, and CIRL/latrophilin, which binds in a calcium-independent manner. Geppert et al. (1998) isolated the mouse neurexin I-alpha gene and found that it contains a large first exon of more

than 1.5 kb that extends to the first site of alternative splicing in the coding region. To evaluate the importance of neurexin I- α in α -latrotoxin action, Geppert et al. (1998) generated mice carrying a deletion of the first exon of the neurexin I- α gene. Homozygous mutant mice lacked neurexin I- α , although the levels of neurexin I- β were unaffected. The mutant mice were viable and fertile, and were indistinguishable in appearance from wildtype animals. The only abnormality observed was that female knockout mice were less able to attend to litters, leading to the death of more pups independent of pup genotype. Geppert et al. (1998) found that α -latrotoxin binding to brain membranes from mutant mice was decreased by almost 50% compared with wildtype membranes. In cultured hippocampal neurons from mutant mice, the toxin was still capable of activating neurotransmission. However, measurements of glutamate release from synaptosomes indicated a major decrease in the amount of release triggered by α -latrotoxin in the presence of calcium. The authors concluded that neurexin I- α is not essential for α -latrotoxin action but contributes to toxin action when calcium is present. They suggested that the action of α -latrotoxin may be me-

diated by independent parallel pathways.

[12460] It is appreciated that the abovementioned animal model for NRXN1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[12461] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12462] Geppert, M.; Khvotchev, M.; Krasnoperov, V.; Goda, Y.; Missler, M.; Hammer, R. E.; Ichtchenko, K.; Petrenko, A. G.; Sudhof, T. C. : Neurexin I-alpha is a major alpha-latrotoxin receptor that cooperates in alpha-latrotoxin action. J. Biol. Chem. 273: 1705-1710, 1998. ; and

[12463] Ushkaryov, Y. A.; Petrenko, A. G.; Geppert, M.; Sudhof, T. C. : Neurexins: synaptic cell surface proteins related to the alpha-latrotoxin receptor and laminin. Science 257: 50-56, 199.

[12464] Further studies establishing the function and utilities of NRXN1 are found in John Hopkins OMIM database record ID 600565, and in sited publications numbered 8169-8173, 673 and 9525-9528 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pleckstrin Homology, Sec7 and Coiled/

coil Domains 3 (PSCD3, Accession NM_004227) is another VGAM191 host target gene. PSCD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSCD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSCD3 BINDING SITE, designated SEQ ID:10423, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12465] Another function of VGAM191 is therefore inhibition of Pleckstrin Homology, Sec7 and Coiled/coil Domains 3 (PSCD3, Accession NM_004227), a gene which regulates vesicle trafficking in eukaryotic cells. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSCD3. The function of PSCD3 has been established by previous studies. ADP-ribosylation factors, or ARFS (see OMIM Ref. No. ARF1; 103180), are small GTP-binding proteins within the Ras superfamily that regulate vesicle trafficking in eukaryotic cells. ARF1 recruits coat proteins (e.g., COPA; 601924) to membranes on the cytoplasmic face of the Golgi apparatus. The PSCD proteins (e.g., PSCD1;

182115), a family of proteins containing a C-terminal pleckstrin homology (PH) domain and a central 200-amino acid region similar to a domain within the yeast Sec7 protein, which is required for vesicular traffic of polypeptides through the Golgi, function as guanine-nucleotide exchange factors (GEFs) for ARFs. Klarlund et al. (1997) identified a cDNA encoding mouse Grp1 (general receptor for phosphoinositides-1) by screening mouse adipocyte and brain cDNA expression libraries with phosphoinositide probes. By searching an EST database for sequences similar to mouse brain Grp1, followed by PCR and screening of a human blood cDNA library, Venkateswarlu et al. (1998) obtained a cDNA encoding PSCD3, which they called GRP1. Sequence analysis showed that the predicted 399-amino acid PSCD3 protein contains a 39-amino acid coiled-coil domain, a 172-amino acid Sec7 domain, and a 118-amino acid PH domain. PSCD3 shares 82.7% and 79.5% amino acid identity with PSCD1 and PSCD2 (OMIM Ref. No. 602488), respectively, as well as 98.8% identity with mouse Grp1. By Scatchard and mutational analyses, Venkateswarlu et al. (1998) determined that PSCD3 binds via its PH domain to the inositol head group of phosphatidylinositol 3,4,5-triphosphate with

high affinity. Confocal laser microscopy demonstrated that stimulation of cells with either epidermal growth factor (EGF; 131530) or nerve growth factor (NGF; 162030) results in PH domain-dependent translocation of PSCD3 from the cytosol to the plasma membrane. The translocation was rapid and transient with EGF, whereas NGF mediated a relatively longer translocation. By searching an EST database for Sec7 domain-related sequences and by screening a placenta cDNA library, Franco et al. (1998) isolated a cDNA encoding PSCD3, which they called ARNO3. Northern blot analysis revealed that PSCD3, in contrast to the ubiquitously expressed PSCD1 and PSCD2, is expressed as a 4.5-kb transcript that is almost absent from liver, thymus, and peripheral blood lymphocytes. Franco et al. (1998) found that PSCD3, like PSCD1 and PSCD2, shows GEF activity, mediated by the Sec7 domain, towards ARF1 but not ARF6 (OMIM Ref. No. 600464). Immunofluorescence microscopy indicated that overexpression of PSCD3 induces major morphologic alterations of the Golgi apparatus, including redistribution of Golgi resident proteins and the coat protein COPB (OMIM Ref. No. 600959). Lietzke et al. (2000) and Ferguson et al. (2000) determined the structure of the GRP1 PH domain in the

unliganded form and bound to inositol

1,3,4,5-tetraphosphate. Lietzke et al. (2000) found that a novel mode of phosphoinositide recognition involving a 20-residue insertion within the beta-6/beta-7 loop explains the unusually high specificity of the GRP1 PH domain and the promiscuous 3-phosphoinositide binding typical of several other PH domains, including that of protein kinase B (AKT1; 164730). By comparing the GRP1 PH domain to other PH domains, general determinants of 3-phosphoinositide recognition and specificity could be deduced. The International Radiation Hybrid Mapping Consortium mapped the PSCD3 gene to chromosome 7 (SHGC-35947).

[12466] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12467] Ferguson, K. M.; Kavran, J. M.; Sankaran, V. G.; Fournier, E.; Isakoff, S. J.; Skolnik, E. Y.; Lemmon, M. A. : Structural basis for discrimination of 3-phosphoinositides by pleckstrin homology domains. *Molec. Cell* 6: 373-384, 2000. ; and

[12468] Franco, M.; Boretto, J.; Robineau, S.; Monier, S.; Goud, B.; Chardin, P.; Chavrier, P. : ARNO3, a Sec7-domain guanine

nucleotide exchange factor for ADP ribosylation factor 1, is involv.

[12469] Further studies establishing the function and utilities of PSCD3 are found in John Hopkins OMIM database record ID 605081, and in cited publications numbered 6807–6809, 490 and 6596 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Recombination Activating Gene 1 (RAG1, Accession NM_000448) is another VGAM191 host target gene. RAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAG1 BINDING SITE, designated SEQ ID:6037, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12470] Another function of VGAM191 is therefore inhibition of Recombination Activating Gene 1 (RAG1, Accession NM_000448). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAG1. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 5 (RPS6KA5, Accession

NM_004755) is another VGAM191 host target gene. RPS6KA5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPS6KA5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA5 BINDING SITE, designated SEQ ID:11144, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12471] Another function of VGAM191 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 5 (RPS6KA5, Accession NM_004755), a gene which plays an essential role in the proliferation of yeast cells. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA5. The function of RPS6KA5 has been established by previous studies. Members of the extracellular signal-regulated kinase (ERK) subfamily of the mitogen-activated protein kinases (MAPKs) are activated by growth factors (see OMIM Ref. No. ERK2, 176948), while stress-activated protein kinase (SAPK) subfamily members are strongly activated by stress signals (see OMIM Ref. No.

SAPK4, 602899). MAPKAP-K1 (see OMIM Ref. No. RPS6KA1, 601684) isoforms appear to be in vivo substrates for ERKs, while MAPKAP-K2 (OMIM Ref. No. 602006) and MAPKAP-K3 (OMIM Ref. No. 602130) are in vivo substrates for SAPK2A (OMIM Ref. No. 600289) and SAPK2B (OMIM Ref. No. 602898). The MAPKAP-K1 proteins each contain 2 protein kinase domains within a single polypeptide, and 1 role of the C-terminal kinase domain is to activate the N-terminal kinase domain. By searching an EST database with the sequence of the MAPKAP-K1 N-terminal kinase domain, Deak et al. (1998) identified cDNAs encoding 2 novel kinases: mitogen- and stress-activated protein kinase-1 (MSK1) and mitogen- and stress-activated protein kinase-2 (OMIM Ref. No. 603606). The predicted 802-amino acid MSK1 protein contains 2 protein kinase domains, each of which includes the 11 subdomains characteristic of all protein kinases. MSK1 shares 43% protein sequence identity with the MAPKAP-K1 isoforms. Northern blot analysis indicated that MSK1 was expressed as a 4-kb mRNA in all tissues tested, with the highest levels of expression in brain, muscle, and placenta. Immunoelectron microscopy localized MSK1 to the nucleus. MSK1 was activated in vitro and in vivo by ei-

ther ERK or SAPK2 proteins. Deak et al. (1998) presented evidence suggesting that MSK1, rather than MAPKAP-K1 or MAPKAP-K2/K3, mediates activation of the cAMP response element-binding protein (see OMIM Ref. No. CREB1, 123810) and activating transcription factor-1 (OMIM Ref. No. 123803) by either growth factors or stress signals. By radiation hybrid analysis, Jiang et al. (1999) mapped the RPS6KA5 gene to chromosome 14q31-q32.

[12472] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12473] Deak, M.; Clifton, A. D.; Lucocq, J. M.; Alessi, D. R. : Mitogen- and stress-activated protein kinase-1 (MSK1) is directly activated by MAPK and SAPK2/p38, and may mediate activation of CREB. EMBO J. 17: 4426-4441, 1998. ; and

[12474] Jiang, C.; Yu, L.; Tu, Q.; Zhao, Y.; Zhang, H.; Zhao, S. : Assignment of a member of the ribosomal protein S6 kinase family, RPS6KA5, to human chromosome 14q31-q32.1 by radiation hybrid map.

[12475] Further studies establishing the function and utilities of RPS6KA5 are found in John Hopkins OMIM database record ID 603607, and in cited publications numbered

2883–2884 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor, Arginine/serine-rich 7, 35kDa (SFRS7, Accession XM_002575) is another VGAM191 host target gene. SFRS7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRS7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS7 BINDING SITE, designated SEQ ID:29899, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12476] Another function of VGAM191 is therefore inhibition of Splicing Factor, Arginine/serine-rich 7, 35kDa (SFRS7, Accession XM_002575), a gene which is required for pre-mRNA splicing. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS7. The function of SFRS7 has been established by previous studies. Cavaloc et al. (1994) used a monoclonal antibody to identify a splicing factor of 35 kD which they named 9G8. Based on partial sequence of tryptic peptides, the authors designed degenerate PCR primers and obtained a PCR product

which was used to probe genomic and cDNA libraries. The isolation and characterization of cDNA clones indicated that the 9G8 protein (gene symbol, SFRS7) is a member of the serine/arginine (SR) splicing factor family because it includes an N-terminal RNA binding domain and a C-terminal SR domain. Members of this family are thought to play key roles in alternative splicing. The RNA binding domain of 9G8 is closely related (79 to 71% identity) to those of the SR factors human SRp20 (OMIM Ref. No. 603364) and *Drosophila* RBP1. Immunodepletion of the 9G8 protein from a nuclear extract resulted in the loss of splicing activity. In turn, in vitro-expressed recombinant 9G8 protein rescued the splicing activity of a 9G8-depleted nuclear extract. Popielarz et al. (1995) isolated and characterized the human 9G8 gene. The gene spans 7,745 bp and consists of 8 exons and 7 introns within the coding sequence, thus contrasting with the organization of some other genes of the SR splicing factor family. By isotopic in situ hybridization, they localized the gene to 2p22-p21. The 5-prime flanking region is GC-rich and contains basal promoter sequences and potential regulatory elements. They presented results raising the possibility that alternative splicing of intron 3 provides a mechanism for modu-

lation of the 9G8 function.

[12477] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12478] Cavaloc, Y.; Popielarz, M.; Fuchs, J.-P.; Gattoni, R.; Stevenin, J. : Characterization and cloning of the human splicing factor 9G8: a novel 35 kDa factor of the serine/ arginine protein family. EMBO J. 13: 2639–2649, 1994. ; and

[12479] Popielarz, M.; Cavaloc, Y.; Mattei, M.-G.; Gattoni, R.; Stevenin, J. : The gene encoding human splicing factor 9G8: structure, chromosomal localization, and expression of alternatively pro.

[12480] Further studies establishing the function and utilities of SFRS7 are found in John Hopkins OMIM database record ID 600572, and in cited publications numbered 9532–9533 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 2 (SMARCA2, Accession NM_003070) is another VGAM191 host target gene. SMARCA2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by

SMARCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCA2 BINDING SITE, designated SEQ ID:9034, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12481] Another function of VGAM191 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A, Member 2 (SMARCA2, Accession NM_003070), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCA2. The function of SMARCA2 has been established by previous studies. Mammalian SWI/SNF complexes are ATP-dependent chromatin remodeling enzymes that have been implicated in the regulation of gene expression, cell cycle control, and oncogenesis. MyoD (MYOD1; 159970) is a muscle-specific regulator capable of inducing myogenesis in numerous cell types. To ascertain the requirement for chromatin remodeling enzymes in cellular differentiation processes, de la Serna et al.

(2001) examined MyoD-mediated induction of muscle differentiation in fibroblasts expressing dominant-negative versions of the human brahma-related gene-1 (BRG1; 603254) or human brahma, the ATPase subunits of 2 distinct SWI/SNF enzymes. They found that induction of the myogenic phenotype was completely abrogated in the presence of the mutant enzymes. They further demonstrated that failure to induce muscle-specific gene expression correlated with inhibition of chromatin remodeling in the promoter region of an endogenous muscle-specific gene. The results demonstrated that SWI/SNF enzymes promote MyoD-mediated muscle differentiation and indicated that these enzymes function by altering chromatin structure in promoter regions of endogenous, differentiation-specific loci. Hakimi et al. (2002) reported the isolation of a human SNF2-containing chromatin remodeling complex that encompasses components of the cohesin and NURD (see OMIM Ref. No. 603526) complexes. They showed that the RAD21 (OMIM Ref. No. 606462) subunit of the cohesin complex directly interacts with the ATPase subunit SNF2. Mapping of RAD21, SNF2, and Mi2 (see OMIM Ref. No. 603277) binding sites by chromatin immunoprecipitation experiments revealed the

specific association of these 3 proteins with human DNA elements containing alu sequences. Hakimi et al. (2002) found a correlation between modification of histone tails and association of the SNF2/cohesin complex with chromatin. In addition, they showed that the association of the cohesin complex with chromatin can be regulated by the state of DNA methylation. Finally, they presented evidence pointing to a role for the ATPase activity of SNF2 in the loading of RAD21 on chromatin.

[12482] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12483] de la Serna, I. L.; Carlson, K. A.; Imbalzano, A. N. : Mammalian SWI/SNF complexes promote MyoD-mediated muscle differentiation. *Nature Genet.* 27: 187–190, 2001.
; and

[12484] Hakimi, M.–A.; Bochar, D. A.; Schmiesing, J. A.; Dong, Y.; Barak, O. G.; Speicher, D. W.; Yokomori, K.; Shiekhattar, R. : A chromatin remodelling complex that loads cohesin onto human.

[12485] Further studies establishing the function and utilities of SMARCA2 are found in John Hopkins OMIM database record ID 600014, and in cited publications numbered

11144, 8358–836 and 804 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Sorting Nexin 9 (SNX9, Accession NM_016224) is another VGAM191 host target gene. SNX9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNX9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX9 BINDING SITE, designated SEQ ID:18328, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12486] Another function of VGAM191 is therefore inhibition of Sorting Nexin 9 (SNX9, Accession NM_016224). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX9. TATA Box Binding Protein (TBP)–associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM_005679) is another VGAM191 host target gene. TAF1C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TAF1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of TAF1C BINDING SITE, designated SEQ ID:12235, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12487] Another function of VGAM191 is therefore inhibition of TATA Box Binding Protein (TBP)–associated Factor, RNA Polymerase I, C, 110kDa (TAF1C, Accession NM_005679), a gene which belongs to component of the RNA polymerase I and II SL1 transcription factor. Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAF1C. The function of TAF1C has been established by previous studies. Using immunoaffinity chromatography with anti–TBP, followed by SDS–PAGE analysis, Comai et al. (1994) isolated the purified 110–kD subunit of SL1. By screening teratocarcinoma and HeLa cell cDNA libraries using degenerate PCR primers corresponding to peptide sequences of the 110–kD subunit of SL1, they obtained a cDNA encoding TAF1C, which they called TAFI110. Comai et al. (1994) also obtained cDNAs encoding TAF1A (OMIM Ref. No. 604903) and TAF1B (OMIM Ref. No. 604904). TAF1C encodes a deduced 869–amino acid protein. West–

ern blot analysis confirmed that TAF1C is expressed as a 110-kD protein. Analysis of SL1 subunit interactions showed that all 3 TAF1 proteins bind to TBP and to each other. However, binding of the SL1 complex to TBP excluded binding of the RNA polymerase II transcription factor TFIID (see OMIM Ref. No. TAF2A; 313650) to TBP. Comai et al. (1994) concluded that this mutually exclusive binding directs the formation of promoter- and RNA polymerase-selective TBP-TAF complexes. The International Radiation Hybrid Mapping Consortium mapped the TAF1C gene to 16q (OMIM Ref. No. L39059). Di Pietro et al. (2000) mapped the TAF1C gene to chromosome 16q24 by fluorescence in situ hybridization.

- [12488] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [12489] Comai, L.; Zomerdijs, J. C. B. M.; Beckmann, H.; Zhou, S.; Admon, A.; Tjian, R. : Reconstitution of transcription factor SL1: exclusive binding of TBP by SL1 or TFIID subunits. *Science* 266: 1966–1972, 1994. ; and
- [12490] Di Pietro, C.; Rapisarda, A.; Amico, V.; Bonaiuto, C.; Viola, A.; Scalia, M.; Motta, S.; Amato, A.; Engel, H.; Messina, A.; Sichel, G.; Grzeschik, K.-H.; Purrello, M. : Genomic local-

iza.

[12491] Further studies establishing the function and utilities of TAF1C are found in John Hopkins OMIM database record ID 604905, and in cited publications numbered 2910–2911 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072) is another VGAM191 host target gene. C1QR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QR1 BINDING SITE, designated SEQ ID:14331, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12492] Another function of VGAM191 is therefore inhibition of Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QR1. FLJ22174 (Accession NM_021945) is another VGAM191

host target gene. FLJ22174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22174 BINDING SITE, designated SEQ ID:22466, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12493] Another function of VGAM191 is therefore inhibition of FLJ22174 (Accession NM_021945). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22174. KIAA0446 (Accession XM_044155) is another VGAM191 host target gene. KIAA0446 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0446, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0446 BINDING SITE, designated SEQ ID:34154, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12494] Another function of VGAM191 is therefore inhibition of KIAA0446 (Accession XM_044155). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0446. KIAA1211 (Accession XM_044178) is another VGAM191 host target gene. KIAA1211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1211 BINDING SITE, designated SEQ ID:34160, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12495] Another function of VGAM191 is therefore inhibition of KIAA1211 (Accession XM_044178). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1211. Kelch-like 8 (Drosophila) (KLHL8, Accession XM_031735) is another VGAM191 host target gene. KLHL8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL8, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL8 BINDING SITE, designated SEQ ID:31475, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12496] Another function of VGAM191 is therefore inhibition of Kelch-like 8 (Drosophila) (KLHL8, Accession XM_031735). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL8. POU Domain, Class 4, Transcription Factor 2 (POU4F2, Accession NM_004575) is another VGAM191 host target gene. POU4F2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU4F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU4F2 BINDING SITE, designated SEQ ID:10919, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12497] Another function of VGAM191 is therefore inhibition of POU Domain, Class 4, Transcription Factor 2 (POU4F2, Accession NM_004575). Accordingly, utilities of VGAM191

include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU4F2.

LOC152756 (Accession XM_098262) is another VGAM191 host target gene. LOC152756 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152756, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152756 BINDING SITE, designated SEQ ID:41551, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12498] Another function of VGAM191 is therefore inhibition of LOC152756 (Accession XM_098262). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152756. LOC196528 (Accession XM_113745) is another VGAM191 host target gene. LOC196528 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196528, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC196528 BINDING SITE, designated SEQ ID:42404, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12499] Another function of VGAM191 is therefore inhibition of LOC196528 (Accession XM_113745). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196528. LOC219529 (Accession XM_167563) is another VGAM191 host target gene. LOC219529 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219529 BINDING SITE, designated SEQ ID:44673, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12500] Another function of VGAM191 is therefore inhibition of LOC219529 (Accession XM_167563). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219529. LOC221751 (Accession XM_166370) is another VGAM191 host target gene. LOC221751 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221751, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221751 BINDING SITE, designated SEQ ID:44188, to the nucleotide sequence of VGAM191 RNA, herein designated VGAM RNA, also designated SEQ ID:2902.

[12501] Another function of VGAM191 is therefore inhibition of LOC221751 (Accession XM_166370). Accordingly, utilities of VGAM191 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221751. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 192 (VGAM192) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12502] VGAM192 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM192 was detected is described hereinabove with reference to Figs. 1-8.

[12503] VGAM192 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12504] VGAM192 gene encodes a VGAM192 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM192 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM192 precursor RNA is designated SEQ ID:178, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:178 is located at position 73488 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12505] VGAM192 precursor RNA folds onto itself, forming VGAM192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12506] An enzyme complex designated DICER COMPLEX, `dices` the VGAM192 folded precursor RNA into VGAM192 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM192 RNA is designated SEQ ID:2903, and is provided hereinbelow with reference to the sequence listing part.

[12507] VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM192 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12508] VGAM192 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM192 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM192 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM192 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12509] The complementary binding of VGAM192 RNA, herein designated VGAM RNA, to host target binding sites on VGAM192 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM192 host target RNA into VGAM192 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12510] It is appreciated that VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM192 host target genes. The mRNA of each one of this plurality of VGAM192 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM192 RNA, herein designated VGAM RNA, and which when bound by VGAM192 RNA causes inhibition of translation of respective one or more VGAM192 host target proteins.

[12511] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM192 gene, herein designated VGAM GENE, on one or more VGAM192 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12512] It is yet further appreciated that a function of VGAM192 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM192 correlate with, and may be deduced from, the identity of the host target genes which VGAM192 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12513] Nucleotide sequences of the VGAM192 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM192 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM192 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM192 are further described hereinbelow with reference to Table 1.

[12514] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM192 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM192 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12515] As mentioned hereinabove with reference to Fig. 1, a function of VGAM192 gene, herein designated VGAM is inhibition of expression of VGAM192 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM192 correlate with, and may be deduced from, the identity of the target genes which VGAM192 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12516] C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM_013252) is a VGAM192 host target gene. CLECSF5 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by CLECSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLECSF5 BINDING SITE, designated SEQ ID:14922, to the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA, also designated SEQ ID:2903.

[12517] A function of VGAM192 is therefore inhibition of C-type (calcium dependent, carbohydrate-recognition domain) Lectin, Superfamily Member 5 (CLECSF5, Accession NM_013252). Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLECSF5. Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM_167853) is another VGAM192 host target gene. NUMA1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NUMA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUMA1 BINDING SITE, designated SEQ ID:44880, to the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA,

also designated SEQ ID:2903.

[12518] Another function of VGAM192 is therefore inhibition of Nuclear Mitotic Apparatus Protein 1 (NUMA1, Accession XM_167853), a gene which is nuclear mitotic apparatus protein. Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUMA1. The function of NUMA1 has been established by previous studies. The NuMA protein was one of the first to be described as a cell cycle-related protein based on a distinct immunofluorescent staining pattern: in interphase, NuMA is present throughout the nucleus, and in mitosis, it localizes to the spindle apparatus (Lydersen and Pettijohn, 1980). Some patients with autoimmune disease have antibodies directed against the NuMA protein. The full-length NUMA cDNA (Compton et al., 1992; Yang et al., 1992) predicts a protein with the largest known coiled-coil region in a protein. By fluorescence in situ hybridization, Sparks et al. (1993) demonstrated that the NUMA1 gene is present in single copy and located on 11q13. Acute promyelocytic leukemia (APL) is uniquely associated with chromosomal translocations that disrupt the gene encoding the retinoic acid receptor, RARA (OMIM Ref. No. 180240). In more than

99% of cases, this disruption results in the formation of a fusion of the RARA gene with the PML gene (OMIM Ref. No. 102578). In rare variants of APL, the RARA gene has been found to be fused to 1 of 2 other genes, PLZF (OMIM Ref. No. 176797) and NPM (OMIM Ref. No. 164040). Although RARA dysregulation is evidently important in APL, the role of the various fusion partners is unclear. Wells et al. (1997) characterized a fourth APL gene fusion, which linked exons encoding the retinoic acid and DNA-binding domains of RARA to 5-prime exons of NUMA1. The NUMA/RARA fusion protein existed in sheet-like nuclear aggregates with which normal NUMA partly colocalized. In contrast to t(15;17) APL (the usual variety) the intracellular distribution of PML was normal in these cells. Wells et al. (1997) suggested that interference with retinoid signaling, and not disruption of PML organization, is essential to the APL phenotype. Their work implicated for the first time an element of the mitotic apparatus in the molecular pathogenesis of human malignancy. The proband of their study was a Caucasian male first seen at 6 months of age for investigation of multiple cutaneous lesions. Despite this unusual clinical presentation, peripheral blood morphology and cell-surface immunophenotype were typical of APL.

Routine analysis of diagnostic bone marrow revealed a clonal cytogenetic abnormality, t(11;17)(q13;q21). The patient was treated with all-trans retinoic acid and achieved complete remission; he remained in morphologic remission 38 months after autologous bone marrow transplantation.

[12519] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12520] Lydersen, B. K.; Pettijohn, D. E. : Human-specific nuclear protein that associates with the polar region of the mitotic apparatus: distribution in a human/hamster hybrid cell. Cell 22: 489-499, 1980. ; and

[12521] Wells, R. A.; Catzavelos, C.; Kamel-Reid, S. : Fusion of retinoic acid receptor alpha to NuMA, the nuclear mitotic apparatus protein, by a variant translocation in acute promyelocytic I.

[12522] Further studies establishing the function and utilities of NUMA1 are found in John Hopkins OMIM database record ID 164009, and in cited publications numbered 2246-2252 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 146 (ZNF146, Accession NM_007145) is an-

other VGAM192 host target gene. ZNF146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF146 BINDING SITE, designated SEQ ID:13994, to the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA, also designated SEQ ID:2903.

[12523] Another function of VGAM192 is therefore inhibition of Zinc Finger Protein 146 (ZNF146, Accession NM_007145), a gene which binds zinc ions, DNA, and heparin. Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF146. The function of ZNF146 has been established by previous studies. Ferbus et al. (1996) reported the characterization of the human OZF protein. The protein produced in E. coli binds zinc ions, DNA, and heparin. These binding activities are characteristic of zinc finger proteins. Immunochemical analysis using antibodies produced against the recombinant protein detected its expression in human mammary epithelial cells but not in stroma cells, which is consistent with the pattern of ex-

pression observed at the RNA level within cell cultures. Western blot analysis demonstrated the expression of a 33-kD nuclear protein similar in size to the predicted protein and, therefore, excluded the presence of an additional transfer-activating domain. The data established the unique structure of the OZF protein which is distinct from previously identified zinc finger proteins. In addition, OZF protein overexpression was found in a tumor cell line, which suggests a possible involvement in carcinogenesis

[12524] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12525] Le Chalony, C.; Prosperi, M.-T.; Haluza, R.; Apiou, F.; Dutrillaux, B.; Goubin, G. : The OZF gene encodes a protein consisting essentially of zinc-finger motifs. J. Molec. Biol. 236: 399-404, 1994. ; and

[12526] Ferbus, D.; Le Chalony, C.; Prosperi, M.-T.; Muleris, M.; Vincent-Salomon, A.; Goubin, G. : Identification, nuclear localization, and binding activities of OZF, a human protein solely compo.

[12527] Further studies establishing the function and utilities of ZNF146 are found in John Hopkins OMIM database record ID 601505, and in cited publications numbered

9488–9490 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.VI

(Accession NM_013443) is another VGAM192 host target gene. VI BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VI BINDING SITE, designated SEQ ID:15108, to the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA, also designated SEQ ID:2903.

[12528] Another function of VGAM192 is therefore inhibition of VI (Accession NM_013443). Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VI. LOC152263 (Accession XM_098195) is another VGAM192 host target gene. LOC152263 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152263 BINDING SITE, designated SEQ ID:41482, to the nucleotide se-

quence of VGAM192 RNA, herein designated VGAM RNA, also designated SEQ ID:2903.

[12529] Another function of VGAM192 is therefore inhibition of LOC152263 (Accession XM_098195). Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152263. LOC169966 (Accession XM_093010) is another VGAM192 host target gene. LOC169966 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169966, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169966 BINDING SITE, designated SEQ ID:40165, to the nucleotide sequence of VGAM192 RNA, herein designated VGAM RNA, also designated SEQ ID:2903.

[12530] Another function of VGAM192 is therefore inhibition of LOC169966 (Accession XM_093010). Accordingly, utilities of VGAM192 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169966. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 193 (VGAM193) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12531] VGAM193 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM193 was detected is described hereinabove with reference to Figs. 1–8.

[12532] VGAM193 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12533] VGAM193 gene encodes a VGAM193 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM193 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM193 precursor RNA is designated SEQ ID:179, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:179 is located at position 94372 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform

virus).

[12534] VGAM193 precursor RNA folds onto itself, forming VGAM193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12535] An enzyme complex designated DICER COMPLEX, `dices` the VGAM193 folded precursor RNA into VGAM193 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM193 RNA is designated SEQ ID:2904, and is provided hereinbelow with reference to the sequence listing part.

[12536] VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM193 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12537] VGAM193 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM193 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM193 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12538] The complementary binding of VGAM193 RNA, herein designated VGAM RNA, to host target binding sites on VGAM193 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM193 host target RNA into VGAM193 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12539] It is appreciated that VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM193 host target genes. The mRNA of each one of this plurality of VGAM193 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM193 RNA, herein designated VGAM RNA, and which when bound by VGAM193 RNA causes inhibition of translation of respective one or more VGAM193 host target proteins.

[12540] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM193 gene, herein designated VGAM GENE, on one or more VGAM193 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12541] It is yet further appreciated that a function of VGAM193 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific func-

tions, and accordingly utilities, of VGAM193 correlate with, and may be deduced from, the identity of the host target genes which VGAM193 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12542] Nucleotide sequences of the VGAM193 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM193 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM193 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM193 are further described hereinbelow with reference to Table 1.

[12543] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM193 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM193 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12544] As mentioned hereinabove with reference to Fig. 1, a function of VGAM193 gene, herein designated VGAM is inhibition of expression of VGAM193 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM193 correlate with, and may be deduced from, the identity of the target genes which VGAM193 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12545] Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM_003674) is a VGAM193 host target gene. CDK10 BINDING SITE1 and CDK10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDK10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK10 BINDING SITE1 and CDK10 BINDING SITE2, designated SEQ ID:9768 and SEQ ID:27557 respectively, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12546] A function of VGAM193 is therefore inhibition of Cyclin-dependent Kinase (CDC2-like) 10 (CDK10, Accession NM_003674), a gene which plays a pivotal role in the regulation of the eukaryotic cell cycle. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK10. The function of CDK10 has been established by previous

studies. Cyclin-dependent kinases (CDKs) are CDC2 (OMIM Ref. No. 116940)-related kinases that bind to cyclin to form active holoenzymes that play a pivotal role in the regulation of the eukaryotic cell cycle. To identify additional CDC2-like protein kinases, Brambilla and Draetta (1994) performed RT-PCR on human tumor cell line mRNA using degenerate oligonucleotides based on regions conserved among CDC2-related proteins. They used a resulting PCR product to screen a HeLa cell library and isolated a partial cDNA encoding a novel protein kinase. The 5-prime end of the cDNA was obtained using RACE. Brambilla and Draetta (1994) designated the predicted 360-amino acid protein PISSLRE, based on the amino acid sequence of the region corresponding to the conserved CDC2 PSTAIRE motif. PISSLRE contains all the structural elements characteristic of CDKs and unique extensions at both ends. Sequence comparisons revealed that it shares 41% and 50% protein sequence identity with CDC2 and CDC2L1 (OMIM Ref. No. 176873), respectively. By Northern blot analysis, the authors determined that PISSLRE was expressed broadly in human tissues as a 2-kb mRNA. An additional 3.5-kb transcript was observed in some tissues. Using a combination of library screening and

5-prime RACE, Grana et al. (1994) isolated PISSLRE cDNAs that differed significantly at both ends from those isolated by Brambilla and Draetta (1994). Brambilla and Draetta (1994) attributed the differences to alternative splicing. Grana et al. (1994) were unable to identify any ATG initiation codons upstream of the sequence encoding the catalytic domain of the putative kinase. They suggested that translation may initiate at 1 of 3 non-ATG initiation codons.

[12547] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12548] Bullrich, F.; MacLachlan, T. K.; Sang, N.; Druck, T.; Veronese, M. L.; Allen, S. L.; Chiorazzi, N.; Koff, A.; Heubner, K.; Croce, C. M.; Giordano, A. : Chromosomal mapping of members of the cdc2 family of protein kinases, cdk3, cdk6, PISSLRE, and PITALRE, and a cdk inhibitor, p27-Kip1, to regions involved in human cancer. *Cancer Res.* 55: 1199-1205, 1995. ; and

[12549] Grana, X.; Claudio, P. P.; De Luca, A.; Sang, N.; Giordano, A. : PISSLRE, a human novel CDC2-related protein kinase. *Oncogene* 9: 2097-2103, 1994.

[12550] Further studies establishing the function and utilities of

CDK10 are found in John Hopkins OMIM database record ID 603464, and in cited publications numbered 288 and 2881 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Elongation of Very Long Chain Fatty Acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 4 (ELOVL4, Accession NM_022726) is another VGAM193 host target gene. ELOVL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELOVL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELOVL4 BINDING SITE, designated SEQ ID:22927, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12551] Another function of VGAM193 is therefore inhibition of Elongation of Very Long Chain Fatty Acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 4 (ELOVL4, Accession NM_022726). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELOVL4. Echinoderm Microtubule Associated Protein Like 1 (EML1, Accession XM_007243) is another VGAM193 host target gene. EML1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EML1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EML1 BINDING SITE, designated SEQ ID:30036, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12552] Another function of VGAM193 is therefore inhibition of Echinoderm Microtubule Associated Protein Like 1 (EML1, Accession XM_007243). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EML1. Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM_003950) is another VGAM193 host target gene. F2RL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F2RL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2RL3 BINDING SITE, designated SEQ ID:10083, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12553] Another function of VGAM193 is therefore inhibition of Coagulation Factor II (thrombin) Receptor-like 3 (F2RL3, Accession NM_003950), a gene which Protease-activated receptor 4; G protein-coupled receptor that increases phosphoinositide hydrolysis. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F2RL3. The function of F2RL3 has been established by previous studies. Protease-activated receptors 1 (PAR1; 187930), 2 (PAR2; 600933), and 3 (PAR3; 601919) are members of a unique G protein-coupled receptor family. They are characterized by a tethered peptide ligand at the extracellular amino terminus that is generated by minor proteolysis. Xu et al. (1998) identified a partial cDNA sequence of a fourth member of this family, PAR4, in an expressed sequence tag (EST) database, and a full-length cDNA clone was isolated from a lymphoma Daudi cell cDNA library. The open reading frame coded for a 7-transmembrane domain protein of 385 amino acids with 33% amino acid sequence identity with PAR1-3. A putative protease cleavage site was identified within the extracellular amino terminus. Northern blot analysis showed that PAR4 mRNA is expressed in a number of human tissues, with high levels

being present in lung, pancreas, thyroid, testis, and small intestine. By fluorescence in situ hybridization, Xu et al. (1998) mapped the PAR4 gene to 19p12. Animal model experiments lend further support to the function of F2RL3. Sambrano et al. (2001) demonstrated that platelets from Par4-deficient mice failed to change shape, mobilize calcium, secrete ATP, or aggregate in response to thrombin.

[12554] It is appreciated that the abovementioned animal model for F2RL3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12555] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12556] Xu, W.-F.; Andersen, H.; Whitmore, T. E.; Presnell, S. R.; Yee, D. P.; Ching, A.; Gilbert, T.; Davie, E. W.; Foster, D. C. : Cloning and characterization of human protease-activated receptor 4. Proc. Nat. Acad. Sci. 95: 6642-6646, 1998. ; and

[12557] Sambrano, G. R.; Weiss, E. J.; Zheng, Y.-W.; Huang, W.; Coughlin, S. R. : Role of thrombin signalling in platelets in haemostasis and thrombosis. Nature 413: 74-78, 2001.

[12558] Further studies establishing the function and utilities of F2RL3 are found in John Hopkins OMIM database record ID 602779, and in cited publications numbered 7653, 9406–940 and 7654 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 1 Receptor Antagonist (IL1RN, Accession NM_000577) is another VGAM193 host target gene. IL1RN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1RN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RN BINDING SITE, designated SEQ ID:6180, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12559] Another function of VGAM193 is therefore inhibition of Interleukin 1 Receptor Antagonist (IL1RN, Accession NM_000577), a gene which inhibits the activity of il-1 by binding to its receptor. il-1ra has no il-1 like activity. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RN. The function of IL1RN has been established by previous studies. Using a homology-based

PCR approach to identify IL1 receptor-related genes, Lovenberg et al. (1996) identified a cDNA, which they called IL1RRP2, that encodes a 561-amino acid protein with significant sequence identity to the IL1 receptor. Like IL1RRP (OMIM Ref. No. 604494), IL1RRP2 failed to bind IL1-alpha (OMIM Ref. No. 147760) or IL1-beta (OMIM Ref. No. 147720). Dale and Nicklin (1999) showed by radiation hybrid mapping that IL1R2 (OMIM Ref. No. 147811), IL1R1 (OMIM Ref. No. 147810), IL1RL2, IL1RL1 (OMIM Ref. No. 601203), and IL18R1 (OMIM Ref. No. 604494) map to 2q12 and are transcribed in the same direction, with IL1R2 being transcribed towards the cluster

[12560] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12561] Dale, M.; Nicklin, M. J. : Interleukin-1 receptor cluster: gene organization of IL1R2, IL1R1, IL1RL2 (IL-1Rrp2), IL1RL1 (T1/ST2), and IL18R1 (IL-1Rrp) on human chromosome 2q. Genomics 57: 177-179, 1999. ; and

[12562] Lovenberg, T. W.; Crowe, P. D.; Liu, C.; Chalmers, D. T.; Liu, X. J.; Liaw, C.; Clevenger, W.; Oltersdorf, T.; De Souza, E. B.; Maki, R. A. : Cloning of a cDNA encoding a novel interleukin.

[12563] Further studies establishing the function and utilities of IL1RN are found in John Hopkins OMIM database record ID 147679, and in cited publications numbered 465–467, 469, 470–472, 4803–4805, 471 and 4806–4808 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Peroxisomal Farnesylated Protein (PXF, Accession NM_002857) is another VGAM193 host target gene. PXF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PXF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXF BINDING SITE, designated SEQ ID:8751, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12564] Another function of VGAM193 is therefore inhibition of Peroxisomal Farnesylated Protein (PXF, Accession NM_002857), a gene which may function in peroxisomal biogenesis or assembly. Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXF. The function of PXF has been established by previous studies. The co–

valent attachment of prenyl lipids, such as farnesyl or geranylgeranyl groups, by specific transferases is indispensable for the cellular sorting of many proteins. James et al. (1994) identified in hamster a farnesylated protein, called peroxisomal farnesylated protein or PxF, that localized to the outer surface of peroxisomes. Kammerer et al. (1997) found that the protein sequence of PxF is 93% identical to that of HK33, a human protein identified by Braun et al. (1994). Braun et al. (1994) reported that HK33 is a predicted 299-amino acid protein with a mass of 33 kD by SDS-PAGE. Northern blot analysis and RT-PCR revealed that HK33 is expressed ubiquitously as 2.2 to 2.5-kb and 4-kb mRNAs. The fact that the gene was transcribed in all cells and tissues tested indicated its status as a house-keeping gene. Braun et al. (1994) demonstrated that at least 2 different HK33 transcripts result from the use of alternative polyadenylation sites. Kammerer et al. (1997) isolated 4 variant HK33, or PXF, mRNAs produced by alternative splicing. They found that the proteins encoded by 2 of the splice variants were farnesylated in vitro. Using immunoelectron microscopy, Kammerer et al. (1997) showed that PXF is localized to the cytoplasmic surface of peroxisomes in liver cells. These authors reported that the

PXF gene contains 8 exons and spans approximately 9 kb. The basal promoter is located within the first 239 bp upstream of the coding region.

[12565] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12566] Braun, A.; Kammerer, S.; Weissenhorn, W.; Weiss, E. H.; Cleve, H. : Sequence of a putative human housekeeping gene (HK33) localized on chromosome 1. Gene 146: 291–295, 1994. ; and

[12567] Kammerer, S.; Arnold, N.; Gutensohn, W.; Mewes, H.–W.; Kunau, W.–H.; Hofler, G.; Roscher, A. A.; Braun, A. : Genomic organization and molecular characterization of a gene encoding HsPX.

[12568] Further studies establishing the function and utilities of PXF are found in John Hopkins OMIM database record ID 600279, and in cited publications numbered 8427–843 and 7739 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DCOHM (Accession NM_032151) is another VGAM193 host target gene. DCOHM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCOHM, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCOHM BINDING SITE, designated SEQ ID:25843, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12569] Another function of VGAM193 is therefore inhibition of DCOHM (Accession NM_032151). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCOHM. FLJ32334 (Accession NM_144565) is another VGAM193 host target gene. FLJ32334 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ32334, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ32334 BINDING SITE, designated SEQ ID:29363, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12570] Another function of VGAM193 is therefore inhibition of FLJ32334 (Accession NM_144565). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ32334. KIAA1391 (Accession XM_040866) is another VGAM193 host target gene. KIAA1391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1391 BINDING SITE, designated SEQ ID:33402, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12571] Another function of VGAM193 is therefore inhibition of KIAA1391 (Accession XM_040866). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1391. NY-REN-60 (Accession XM_040506) is another VGAM193 host target gene. NY-REN-60 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NY-REN-60, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NY-REN-60 BINDING SITE, designated SEQ ID:33316, to the

nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12572] Another function of VGAM193 is therefore inhibition of NY-REN-60 (Accession XM_040506). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NY-REN-60. SP329 (Accession NM_030793) is another VGAM193 host target gene. SP329 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SP329, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SP329 BINDING SITE, designated SEQ ID:25099, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12573] Another function of VGAM193 is therefore inhibition of SP329 (Accession NM_030793). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SP329. Testis-specific Kinase 2 (TESK2, Accession XM_032399) is another VGAM193 host target gene. TESK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by TESK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TESK2 BINDING SITE, designated SEQ ID:31649, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12574] Another function of VGAM193 is therefore inhibition of Testis-specific Kinase 2 (TESK2, Accession XM_032399). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TESK2. LOC147622 (Accession XM_097255) is another VGAM193 host target gene. LOC147622 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147622 BINDING SITE, designated SEQ ID:40849, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12575] Another function of VGAM193 is therefore inhibition of

LOC147622 (Accession XM_097255). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147622. LOC155435 (Accession XM_088257) is another VGAM193 host target gene. LOC155435 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155435, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155435 BINDING SITE, designated SEQ ID:39569, to the nucleotide sequence of VGAM193 RNA, herein designated VGAM RNA, also designated SEQ ID:2904.

[12576] Another function of VGAM193 is therefore inhibition of LOC155435 (Accession XM_088257). Accordingly, utilities of VGAM193 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155435. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 194 (VGAM194) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[12577] VGAM194 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM194 was detected is described hereinabove with reference to Figs. 1–8.

[12578] VGAM194 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12579] VGAM194 gene encodes a VGAM194 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM194 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM194 precursor RNA is designated SEQ ID:180, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:180 is located at position 172456 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12580] VGAM194 precursor RNA folds onto itself, forming VGAM194 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[12581] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM194 folded precursor RNA into VGAM194 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 44%) nucleotide se-
quence of VGAM194 RNA is designated SEQ ID:2905, and
is provided hereinbelow with reference to the sequence
listing part.

[12582] VGAM194 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM194 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM194 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12583] VGAM194 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM194 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM194 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12584] The complementary binding of VGAM194 RNA, herein designated VGAM RNA, to host target binding sites on VGAM194 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM194 host target RNA into VGAM194 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12585] It is appreciated that VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM194 host target genes. The mRNA of each one of this plurality of VGAM194 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM194 RNA, herein designated VGAM RNA, and which when bound by VGAM194 RNA causes inhibition of translation of respective one or more VGAM194 host target proteins.

[12586] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM194 gene, herein designated VGAM GENE, on one or more VGAM194 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12587] It is yet further appreciated that a function of VGAM194 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM194 correlate with, and may be deduced from, the identity of the host target genes which VGAM194 binds and inhibits, and the

function of these host target genes, as elaborated herein–below.

[12588] Nucleotide sequences of the VGAM194 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM194 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM194 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM194 are further described hereinbelow with reference to Table 1.

[12589] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM194 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM194 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12590] As mentioned hereinabove with reference to Fig. 1, a function of VGAM194 gene, herein designated VGAM is inhibition of expression of VGAM194 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM194 correlate with, and may be deduced from, the identity of the target genes which VGAM194 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[12591] A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession NM_007200) is a VGAM194 host target gene. AKAP13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP13 BINDING SITE, designated SEQ ID:14055, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12592] A function of VGAM194 is therefore inhibition of A Kinase (PRKA) Anchor Protein 13 (AKAP13, Accession NM_007200), a gene which regulates subcellular localization of type II cAMP-dependent PKA. Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP13. The function of AKAP13 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM17. Charot-Leyden Crystal Protein (CLC, Accession NM_013246) is another VGAM194 host target gene. CLC BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by CLC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLC BINDING SITE, designated SEQ ID:14907, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12593] Another function of VGAM194 is therefore inhibition of Charot-Leyden Crystal Protein (CLC, Accession NM_013246). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLC. Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM_000150) is another VGAM194 host target gene. FUT6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FUT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT6 BINDING SITE, designated SEQ ID:5648, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12594] Another function of VGAM194 is therefore inhibition of

Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM_000150), a gene which is involved in the biosynthesis of the e-selectin ligand, sialyl-lewis x. catalyzes the transfer of fucose from gdp- beta-fucose to alpha-2,3 sialylated substrates. Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT6. The function of FUT6 has been established by previous studies. The alpha-1,3-fucosyltransferases constitute a large family of glycosyltransferases with a high degree of homology. The enzymes of this family comprise 3 main activity patterns called myeloid, plasma, and Lewis, based on their capacity to transfer alpha-L-fucose to distinct oligosaccharide acceptors, their sensitivity to N-ethylmaleimide inhibition, their cation requirements, and their tissue-specific expression patterns. The different categories of alpha-1,3-fucosyltransferases are sequentially expressed during embryo-fetal development.

[12595] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12596] Brinkman-Van der Linden, E. C. M.; Mollicone, R.; Oriol, R.; Larson, G.; Van den Eijnden, D. H.; Van Dijk, W. : A

missense mutation in the FUT6 gene results in total absence of alpha-3-fucosylation of human alpha-1-acid glycoprotein. J. Biol. Chem. 271: 14492-14495, 1996. ; and

[12597] Cameron, H. S.; Szczepaniak, D.; Weston, B. W. : Expression of human chromosome 19p alpha-(1,3)-fucosyltransferase genes in normal tissues: alternative splicing, polyadenylation, and is.

[12598] Further studies establishing the function and utilities of FUT6 are found in John Hopkins OMIM database record ID 136836, and in cited publications numbered 2180, 2983-2984, 2177, 2985-298 and 2179 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 20 Open Reading Frame 19 (C20orf19, Accession NM_018474) is another VGAM194 host target gene. C20orf19 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf19 BINDING SITE, designated SEQ ID:20541, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM

RNA, also designated SEQ ID:2905.

[12599] Another function of VGAM194 is therefore inhibition of Chromosome 20 Open Reading Frame 19 (C20orf19, Accession NM_018474). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf19. DKFZp434O0320 (Accession XM_097012) is another VGAM194 host target gene. DKFZp434O0320 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434O0320, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434O0320 BINDING SITE, designated SEQ ID:40702, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12600] Another function of VGAM194 is therefore inhibition of DKFZp434O0320 (Accession XM_097012). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434O0320. FLJ12934 (Accession NM_022899) is another VGAM194 host target gene. FLJ12934 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12934 BINDING SITE, designated SEQ ID:23173, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12601] Another function of VGAM194 is therefore inhibition of FLJ12934 (Accession NM_022899). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12934. FLJ13441 (Accession NM_023924) is another VGAM194 host target gene. FLJ13441 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13441 BINDING SITE, designated SEQ ID:23389, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12602] Another function of VGAM194 is therefore inhibition of

FLJ13441 (Accession NM_023924). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13441. FLJ20079 (Accession NM_017656) is another VGAM194 host target gene. FLJ20079 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20079, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20079 BINDING SITE, designated SEQ ID:19175, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12603] Another function of VGAM194 is therefore inhibition of FLJ20079 (Accession NM_017656). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20079. KIAA0426 (Accession NM_014724) is another VGAM194 host target gene. KIAA0426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0426 BINDING SITE, designated SEQ ID:16305, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12604] Another function of VGAM194 is therefore inhibition of KIAA0426 (Accession NM_014724). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0426. KIAA1143 (Accession XM_044014) is another VGAM194 host target gene. KIAA1143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1143 BINDING SITE, designated SEQ ID:34074, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12605] Another function of VGAM194 is therefore inhibition of KIAA1143 (Accession XM_044014). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1143. Synaptojanin 2 (SYNJ2, Accession XM_029746)

is another VGAM194 host target gene. SYNJ2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNJ2 BINDING SITE, designated SEQ ID:30941, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12606] Another function of VGAM194 is therefore inhibition of Synaptojanin 2 (SYNJ2, Accession XM_029746). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNJ2. LOC220776 (Accession XM_043388) is another VGAM194 host target gene. LOC220776 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220776, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220776 BINDING SITE, designated SEQ ID:33928, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12607] Another function of VGAM194 is therefore inhibition of LOC220776 (Accession XM_043388). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220776. LOC257239 (Accession XM_173125) is another VGAM194 host target gene. LOC257239 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257239, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257239 BINDING SITE, designated SEQ ID:46372, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12608] Another function of VGAM194 is therefore inhibition of LOC257239 (Accession XM_173125). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257239. LOC90594 (Accession XM_032820) is another VGAM194 host target gene. LOC90594 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90594, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90594 BINDING SITE, designated SEQ ID:31773, to the nucleotide sequence of VGAM194 RNA, herein designated VGAM RNA, also designated SEQ ID:2905.

[12609] Another function of VGAM194 is therefore inhibition of LOC90594 (Accession XM_032820). Accordingly, utilities of VGAM194 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90594. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 195 (VGAM195) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12610] VGAM195 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM195 was detected is described hereinabove with reference to Figs. 1–8.

[12611] VGAM195 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM195 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12612] VGAM195 gene encodes a VGAM195 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM195 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM195 precursor RNA is designated SEQ ID:181, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:181 is located at position 113163 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12613] VGAM195 precursor RNA folds onto itself, forming VGAM195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12614] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM195 folded precursor RNA into VGAM195 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM195 RNA is designated SEQ ID:2906, and is provided hereinbelow with reference to the sequence listing part.

[12615] VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM195 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12616] VGAM195 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM195 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM195 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12617] The complementary binding of VGAM195 RNA, herein designated VGAM RNA, to host target binding sites on VGAM195 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM195 host target RNA into VGAM195 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12618] It is appreciated that VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM195 host target genes. The mRNA of each one of this plurality of VGAM195 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM195 RNA, herein designated VGAM RNA, and which when bound by VGAM195 RNA causes inhibition of translation of respective one or more VGAM195 host target proteins.

[12619] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM195 gene, herein designated VGAM GENE, on one or more VGAM195 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12620] It is yet further appreciated that a function of VGAM195 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM195 correlate with, and may be deduced from, the identity of the host target genes which VGAM195 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12621] Nucleotide sequences of the VGAM195 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM195 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM195 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM195 are further

described hereinbelow with reference to Table 1.

[12622] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM195 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM195 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12623] As mentioned hereinabove with reference to Fig. 1, a function of VGAM195 gene, herein designated VGAM is inhibition of expression of VGAM195 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM195 correlate with, and may be deduced from, the identity of the target genes which VGAM195 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12624] Collagen, Type X, Alpha 1(Schmid metaphyseal chondrodysplasia) (COL10A1, Accession NM_000493) is a VGAM195 host target gene. COL10A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL10A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of COL10A1 BINDING SITE, designated SEQ ID:6105, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12625] A function of VGAM195 is therefore inhibition of Collagen, Type X, Alpha 1(Schmid metaphyseal chondrodysplasia) (COL10A1, Accession NM_000493). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL10A1. COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_004376) is another VGAM195 host target gene. COX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COX15 BINDING SITE, designated SEQ ID:10598, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12626] Another function of VGAM195 is therefore inhibition of COX15 Homolog, Cytochrome C Oxidase Assembly Protein (yeast) (COX15, Accession NM_004376). Accordingly, util-

ities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COX15. Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728) is another VGAM195 host target gene. C20orf110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf110 BINDING SITE, designated SEQ ID:38830, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12627] Another function of VGAM195 is therefore inhibition of Chromosome 20 Open Reading Frame 110 (C20orf110, Accession XM_086728). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf110. CGI-142 (Accession NM_016073) is another VGAM195 host target gene. CGI-142 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGI-142, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-142 BINDING SITE, designated SEQ ID:18147, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12628] Another function of VGAM195 is therefore inhibition of CGI-142 (Accession NM_016073). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-142. DIS3 (Accession NM_014953) is another VGAM195 host target gene. DIS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIS3 BINDING SITE, designated SEQ ID:17302, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12629] Another function of VGAM195 is therefore inhibition of DIS3 (Accession NM_014953). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIS3.

LOC153338 (Accession XM_098361) is another VGAM195 host target gene. LOC153338 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153338, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153338 BINDING SITE, designated SEQ ID:41607, to the nucleotide sequence of VGAM195 RNA, herein designated VGAM RNA, also designated SEQ ID:2906.

[12630] Another function of VGAM195 is therefore inhibition of LOC153338 (Accession XM_098361). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153338. LOC202781 (Accession XM_117455) is another VGAM195 host target gene. LOC202781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202781 BINDING SITE, designated SEQ ID:43444, to the nucleotide sequence of VGAM195 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2906.

[12631] Another function of VGAM195 is therefore inhibition of LOC202781 (Accession XM_117455). Accordingly, utilities of VGAM195 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202781. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 196 (VGAM196) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12632] VGAM196 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM196 was detected is described hereinabove with reference to Figs. 1–8.

[12633] VGAM196 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12634] VGAM196 gene encodes a VGAM196 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM196 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM196 precursor RNA is designated SEQ ID:182, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:182 is located at position 205571 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12635] VGAM196 precursor RNA folds onto itself, forming VGAM196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12636] An enzyme complex designated DICER COMPLEX, `dices` the VGAM196 folded precursor RNA into VGAM196 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM196 RNA is designated SEQ ID:2907, and is provided hereinbelow with reference to the sequence listing part.

[12637] VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM196 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12638] VGAM196 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM196 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM196 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12639] The complementary binding of VGAM196 RNA, herein designated VGAM RNA, to host target binding sites on VGAM196 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM196 host target RNA into VGAM196 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12640] It is appreciated that VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM196 host target genes. The mRNA of each one of this plurality of VGAM196 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM196 RNA, herein designated VGAM RNA, and which when bound by VGAM196 RNA causes inhibition of translation of respective one or more VGAM196 host target proteins.

[12641] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM196 gene, herein designated VGAM GENE, on one or more VGAM196 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[12642] It is yet further appreciated that a function of VGAM196 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM196 correlate with, and may be deduced from, the identity of the host target genes which VGAM196 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12643] Nucleotide sequences of the VGAM196 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM196 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM196 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM196 are further described hereinbelow with reference to Table 1.

[12644] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM196 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM196 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12645] As mentioned hereinabove with reference to Fig. 1, a function of VGAM196 gene, herein designated VGAM is inhibition of expression of VGAM196 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM196 correlate with, and may be deduced from, the identity of the target genes which VGAM196 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12646] ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933) is a VGAM196 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATP8B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32520, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12647] A function of VGAM196 is therefore inhibition of ATPase,

Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. Oculocerebrorenal Syndrome of Lowe (OCRL, Accession NM_000276) is another VGAM196 host target gene. OCRL BINDING SITE1 and OCRL BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OCRL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OCRL BINDING SITE1 and OCRL BINDING SITE2, designated SEQ ID:5819 and SEQ ID:7306 respectively, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12648] Another function of VGAM196 is therefore inhibition of Oculocerebrorenal Syndrome of Lowe (OCRL, Accession NM_000276). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OCRL. Thymine-DNA Glycosylase (TDG, Accession NM_003211) is another VGAM196 host target gene. TDG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by TDG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TDG BINDING SITE, designated SEQ ID:9206, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12649] Another function of VGAM196 is therefore inhibition of Thymine–DNA Glycosylase (TDG, Accession NM_003211), a gene which excises uracil and thymine from mispairs with guanine. Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TDG. The function of TDG has been established by previous studies. The process of spontaneous hydrolytic deamination affects all DNA bases with exocyclic amino groups (Lindahl, 1982). Hydrolytic deamination of 5–methylcytosine leads to the formation of G/T mismatches. These G/T mismatches are corrected to G/C basepairs by a mismatch–specific DNA–binding glycosylase, TDG. TDG initiates repair of G/T and G/U mismatches, commonly associated with CpG islands, by removing thymine and uracil moieties. Tini et al. (2002) reported that TDG associates with transcriptional coacti–

vators CBP (OMIM Ref. No. 600140) and p300 (OMIM Ref. No. 602700) and that the resulting complexes are competent for both the excision step of repair and histone acetylation. TDG stimulated CBP transcriptional activity in transfected cells and reciprocally served as a substrate for CBP/p300 acetylation. This acetylation triggered release of CBP from DNA ternary complexes and also regulated recruitment of repair endonuclease APE (OMIM Ref. No. 107748). These observations revealed a potential regulatory role for protein acetylation in base mismatch repair and a role for CBP/p300 in maintaining genomic stability.

[12650] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12651] Tini, M.; Benecke, A.; Um, S.-J.; Torchia, J.; Evans, R. M.; Chambon, P. : Association of CBP/p300 acetylase and thymine DNA glycosylase links DNA repair and transcription. *Molec. Cell* 9: 265–277, 2002. ; and

[12652] Neddermann, P.; Gallinari, P.; Lettieri, T.; Schmid, D.; Truong, O.; Hsuan, J. J.; Wiebauer, K.; Jiricny, J. : Cloning and expression of human G/T mismatch-specific thymine–DNA glycosyl.

[12653] Further studies establishing the function and utilities of

TDG are found in John Hopkins OMIM database record ID 601423, and in cited publications numbered 9268–927 and 10686 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BICD2 (Accession XM_046863) is another VGAM196 host target gene. BICD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BICD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BICD2 BINDING SITE, designated SEQ ID:34854, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12654] Another function of VGAM196 is therefore inhibition of BICD2 (Accession XM_046863). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BICD2. Reserved (C8orf13, Accession XM_088377) is another VGAM196 host target gene. C8orf13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C8orf13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND–

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf13 BINDING SITE, designated SEQ ID:39654, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12655] Another function of VGAM196 is therefore inhibition of Reserved (C8orf13, Accession XM_088377). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf13. DKFZp434D177 (Accession NM_032264) is another VGAM196 host target gene. DKFZp434D177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434D177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434D177 BINDING SITE, designated SEQ ID:26011, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12656] Another function of VGAM196 is therefore inhibition of DKFZp434D177 (Accession NM_032264). Accordingly, utilities of VGAM196 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with DKFZp434D177. DKFZp761P1010 (Accession NM_018423) is another VGAM196 host target gene. DKFZp761P1010 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZp761P1010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761P1010 BINDING SITE, designated SEQ ID:20479, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12657] Another function of VGAM196 is therefore inhibition of DKFZp761P1010 (Accession NM_018423). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761P1010. FLJ10535 (Accession NM_018129) is another VGAM196 host target gene. FLJ10535 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ10535 BINDING SITE, designated SEQ ID:19922, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12658] Another function of VGAM196 is therefore inhibition of FLJ10535 (Accession NM_018129). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10535. FLJ23186 (Accession XM_017088) is another VGAM196 host target gene. FLJ23186 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23186, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23186 BINDING SITE, designated SEQ ID:30297, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12659] Another function of VGAM196 is therefore inhibition of FLJ23186 (Accession XM_017088). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23186. KIAA0495 (Accession XM_031397) is another VGAM196 host target gene. KIAA0495 BINDING SITE is HOST TARGET

binding site found in the 5` untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31362, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12660] Another function of VGAM196 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA1126 (Accession XM_050325) is another VGAM196 host target gene. KIAA1126 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1126, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1126 BINDING SITE, designated SEQ ID:35611, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12661] Another function of VGAM196 is therefore inhibition of

KIAA1126 (Accession XM_050325). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1126. MKP-7 (Accession XM_039106) is another VGAM196 host target gene. MKP-7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MKP-7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MKP-7 BINDING SITE, designated SEQ ID:33009, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12662] Another function of VGAM196 is therefore inhibition of MKP-7 (Accession XM_039106). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MKP-7. SCDGF-B (Accession NM_033135) is another VGAM196 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:26984 and SEQ ID:24882 respectively, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12663] Another function of VGAM196 is therefore inhibition of SCDGF-B (Accession NM_033135). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCDGF-B. LOC199725 (Accession XM_117119) is another VGAM196 host target gene. LOC199725 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199725 BINDING SITE, designated SEQ ID:43244, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12664] Another function of VGAM196 is therefore inhibition of LOC199725 (Accession XM_117119). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC199725. LOC202459 (Accession NM_145303) is another VGAM196 host target gene. LOC202459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202459 BINDING SITE, designated SEQ ID:29816, to the nucleotide sequence of VGAM196 RNA, herein designated VGAM RNA, also designated SEQ ID:2907.

[12665] Another function of VGAM196 is therefore inhibition of LOC202459 (Accession NM_145303). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202459. LOC257048 (Accession XM_171240) is another VGAM196 host target gene. LOC257048 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257048 BINDING SITE, designated SEQ ID:46028, to the nucleotide sequence of VGAM196 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2907.

[12666] Another function of VGAM196 is therefore inhibition of LOC257048 (Accession XM_171240). Accordingly, utilities of VGAM196 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257048. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 197 (VGAM197) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12667] VGAM197 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM197 was detected is described hereinabove with reference to Figs. 1–8.

[12668] VGAM197 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12669] VGAM197 gene encodes a VGAM197 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM197 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM197 precursor RNA is designated SEQ ID:183, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:183 is located at position 31769 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12670] VGAM197 precursor RNA folds onto itself, forming VGAM197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12671] An enzyme complex designated DICER COMPLEX, `dices` the VGAM197 folded precursor RNA into VGAM197 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 49%) nucleotide sequence of VGAM197 RNA is designated SEQ ID:2908, and is provided hereinbelow with reference to the sequence listing part.

[12672] VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM197 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12673] VGAM197 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM197 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM197 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12674] The complementary binding of VGAM197 RNA, herein designated VGAM RNA, to host target binding sites on VGAM197 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM197 host target RNA into VGAM197 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12675] It is appreciated that VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM197 host target genes. The mRNA of each one of this plurality of VGAM197 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM197 RNA, herein designated VGAM RNA, and which when bound by VGAM197 RNA causes inhibition of translation of respective one or more VGAM197 host target proteins.

[12676] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM197 gene, herein designated VGAM GENE, on one or more VGAM197 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[12677] It is yet further appreciated that a function of VGAM197 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM197 correlate with, and may be deduced from, the identity of the host target genes which VGAM197 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12678] Nucleotide sequences of the VGAM197 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM197 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM197 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM197 are further described hereinbelow with reference to Table 1.

[12679] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM197 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM197 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12680] As mentioned hereinabove with reference to Fig. 1, a function of VGAM197 gene, herein designated VGAM is inhibition of expression of VGAM197 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM197 correlate with, and may be deduced from, the identity of the target genes which VGAM197 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12681] Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729) is a VGAM197 host target gene. DIAPH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIAPH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIAPH2 BINDING SITE, designated SEQ ID:13559, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12682] A function of VGAM197 is therefore inhibition of Di-

aphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729), a gene which may affect in oogenesis. Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIAPH2. The function of DIAPH2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM129.F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_033644) is another VGAM197 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:27368, SEQ ID:14666 and SEQ ID:27378 respectively, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12683] Another function of VGAM197 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_033644), a gene which somehow is involved in the

process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949) is another VGAM197 host target gene. ACTR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACTR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACTR1A BINDING SITE, designated SEQ ID:31536, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12684] Another function of VGAM197 is therefore inhibition of ARP1 Actin-related Protein 1 Homolog A, Centractin Alpha (yeast) (ACTR1A, Accession XM_031949). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with ACTR1A. CED-6 (Accession NM_016315) is another VGAM197 host target gene. CED-6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CED-6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CED-6 BINDING SITE, designated SEQ ID:18432, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12685] Another function of VGAM197 is therefore inhibition of CED-6 (Accession NM_016315). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CED-6. GABA(A) Receptor-associated Protein Like 1 (GABARAPL1, Accession NM_031412) is another VGAM197 host target gene. GABARAPL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GABARAPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABARAPL1 BINDING SITE, designated SEQ ID:25391, to the nucleotide sequence of

VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12686] Another function of VGAM197 is therefore inhibition of GABA(A) Receptor-associated Protein Like 1 (GABARAPL1, Accession NM_031412). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABARAPL1.

MGC15396 (Accession NM_052855) is another VGAM197 host target gene. MGC15396 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15396, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15396 BINDING SITE, designated SEQ ID:27438, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12687] Another function of VGAM197 is therefore inhibition of MGC15396 (Accession NM_052855). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15396. Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651) is another VGAM197 host target gene.

PELI1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PELI1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PELI1 BINDING SITE, designated SEQ ID:21817, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12688] Another function of VGAM197 is therefore inhibition of Pellino Homolog 1 (Drosophila) (PELI1, Accession NM_020651). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PELI1. LOC203411 (Accession XM_117547) is another VGAM197 host target gene. LOC203411 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203411 BINDING SITE, designated SEQ ID:43565, to the nucleotide sequence of VGAM197 RNA, herein designated VGAM RNA, also designated SEQ ID:2908.

[12689] Another function of VGAM197 is therefore inhibition of LOC203411 (Accession XM_117547). Accordingly, utilities of VGAM197 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203411. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 198 (VGAM198) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12690] VGAM198 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM198 was detected is described hereinabove with reference to Figs. 1–8.

[12691] VGAM198 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12692] VGAM198 gene encodes a VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM198

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM198 precursor RNA is designated SEQ ID:184, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:184 is located at position 194945 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12693] VGAM198 precursor RNA folds onto itself, forming VGAM198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12694] An enzyme complex designated DICER COMPLEX, `dices` the VGAM198 folded precursor RNA into VGAM198 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM198 RNA is designated SEQ ID:2909, and is provided hereinbelow with reference to the sequence listing part.

[12695] VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM198 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12696] VGAM198 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM198 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM198 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12697] The complementary binding of VGAM198 RNA, herein designated VGAM RNA, to host target binding sites on VGAM198 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM198 host target RNA into VGAM198 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12698] It is appreciated that VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM198 host target genes. The mRNA of

each one of this plurality of VGAM198 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM198 RNA, herein designated VGAM RNA, and which when bound by VGAM198 RNA causes inhibition of translation of respective one or more VGAM198 host target proteins.

[12699] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM198 gene, herein designated VGAM GENE, on one or more VGAM198 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[12700] It is yet further appreciated that a function of VGAM198 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM198 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM198 correlate with, and may be deduced from, the identity of the host target genes which VGAM198 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12701] Nucleotide sequences of the VGAM198 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM198 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM198 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM198 are further described hereinbelow with reference to Table 1.

[12702] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM198 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM198 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12703] As mentioned hereinabove with reference to Fig. 1, a function of VGAM198 gene, herein designated VGAM is inhibition of expression of VGAM198 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM198 correlate with, and may be deduced from, the identity of the target genes which VGAM198 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12704] FLJ23516 (Accession NM_024539) is a VGAM198 host target gene. FLJ23516 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23516, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23516 BINDING SITE, designated SEQ ID:23747, to the nucleotide sequence of VGAM198 RNA, herein designated VGAM RNA, also designated SEQ ID:2909.

[12705] A function of VGAM198 is therefore inhibition of FLJ23516 (Accession NM_024539). Accordingly, utilities of

VGAM198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23516. LOC148189 (Accession XM_086087) is another VGAM198 host target gene. LOC148189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148189 BINDING SITE, designated SEQ ID:38483, to the nucleotide sequence of VGAM198 RNA, herein designated VGAM RNA, also designated SEQ ID:2909.

[12706] Another function of VGAM198 is therefore inhibition of LOC148189 (Accession XM_086087). Accordingly, utilities of VGAM198 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148189. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 199 (VGAM199) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12707] VGAM199 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM199 was detected is described hereinabove with reference to Figs. 1–8.

[12708] VGAM199 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12709] VGAM199 gene encodes a VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM199 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM199 precursor RNA is designated SEQ ID:185, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:185 is located at position 121113 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12710] VGAM199 precursor RNA folds onto itself, forming VGAM199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[12711] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM199 folded precursor RNA into VGAM199 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 43%) nucleotide se-
quence of VGAM199 RNA is designated SEQ ID:2910, and
is provided hereinbelow with reference to the sequence
listing part.

[12712] VGAM199 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM199 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM199 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[12713] VGAM199 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM199 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM199 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[12714] The complementary binding of VGAM199 RNA, herein designated VGAM RNA, to host target binding sites on VGAM199 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM199 host target RNA into VGAM199 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12715] It is appreciated that VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM199 host target genes. The mRNA of each one of this plurality of VGAM199 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM199 RNA, herein designated VGAM RNA, and which when bound by VGAM199 RNA causes inhibition of translation of respective one or more VGAM199 host target proteins.

[12716] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM199 gene, herein designated VGAM GENE, on one or

more VGAM199 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12717] It is yet further appreciated that a function of VGAM199 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM199 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM199 correlate with, and may be deduced from, the identity of the host target genes which VGAM199 binds and inhibits, and the function of these host target genes, as elaborated herein-

below.

- [12718] Nucleotide sequences of the VGAM199 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM199 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM199 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM199 are further described hereinbelow with reference to Table 1.
- [12719] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM199 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM199 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [12720] As mentioned hereinabove with reference to Fig. 1, a function of VGAM199 gene, herein designated VGAM is inhibition of expression of VGAM199 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM199 correlate with, and may be deduced from, the identity of the target genes which VGAM199 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12721] Catalase (CAT, Accession NM_001752) is a VGAM199 host target gene. CAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAT BINDING SITE, designated SEQ ID:7487, to the nucleotide sequence of VGAM199 RNA, herein designated VGAM RNA, also designated SEQ ID:2910.

[12722] A function of VGAM199 is therefore inhibition of Catalase (CAT, Accession NM_001752). Accordingly, utilities of VGAM199 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAT. FLJ11101 (Accession NM_018322) is another VGAM199 host target gene. FLJ11101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11101 BINDING SITE, designated SEQ ID:20313, to the nucleotide sequence of VGAM199 RNA, herein designated VGAM RNA, also designated SEQ ID:2910.

- [12723] Another function of VGAM199 is therefore inhibition of FLJ11101 (Accession NM_018322). Accordingly, utilities of VGAM199 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11101. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 200 (VGAM200) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.
- [12724] VGAM200 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM200 was detected is described hereinabove with reference to Figs. 1–8.
- [12725] VGAM200 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.
- [12726] VGAM200 gene encodes a VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM200 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM200 precursor RNA is designated SEQ ID:186, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:186 is located at position 92234 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12727] VGAM200 precursor RNA folds onto itself, forming VGAM200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12728] An enzyme complex designated DICER COMPLEX, `dices` the VGAM200 folded precursor RNA into VGAM200 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 59%) nucleotide sequence of VGAM200 RNA is designated SEQ ID:2911, and is provided hereinbelow with reference to the sequence listing part.

[12729] VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM200 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12730] VGAM200 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM200 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM200 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12731] The complementary binding of VGAM200 RNA, herein designated VGAM RNA, to host target binding sites on VGAM200 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM200 host target RNA into VGAM200 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12732] It is appreciated that VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM200 host target genes. The mRNA of each one of this plurality of VGAM200 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM200 RNA, herein designated VGAM RNA, and which when bound by VGAM200 RNA causes inhibition of translation of respective one or more VGAM200 host target proteins.

[12733] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM200 gene, herein designated VGAM GENE, on one or more VGAM200 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12734] It is yet further appreciated that a function of VGAM200 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM200 correlate with, and may be deduced from, the identity of the host target genes which VGAM200 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12735] Nucleotide sequences of the VGAM200 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM200 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM200 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM200 are further described hereinbelow with reference to Table 1.

[12736] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM200 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM200 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[12737] As mentioned hereinabove with reference to Fig. 1, a function of VGAM200 gene, herein designated VGAM is inhibition of expression of VGAM200 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM200 correlate with, and may be deduced from, the identity of the target genes which VGAM200 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12738] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 4 (B4GALT4, Accession NM_003778) is a VGAM200 host target gene. B4GALT4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT4 BINDING SITE, designated SEQ ID:9861, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12739] A function of VGAM200 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypep-

tide 4 (B4GALT4, Accession NM_003778). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT4. Chromosome 14 Open Reading Frame 1 (C14orf1, Accession NM_007176) is another VGAM200 host target gene. C14orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C14orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C14orf1 BINDING SITE, designated SEQ ID:14028, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12740] Another function of VGAM200 is therefore inhibition of Chromosome 14 Open Reading Frame 1 (C14orf1, Accession NM_007176). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C14orf1. Epidermal Growth Factor (beta-urogastrone) (EGF, Accession NM_001963) is another VGAM200 host target gene. EGF BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGF, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGF BINDING SITE, designated SEQ ID:7689, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12741] Another function of VGAM200 is therefore inhibition of Epidermal Growth Factor (beta-urogastrone) (EGF, Accession NM_001963), a gene which stimulates the growth of epidermal and epithelial tissues and of some fibroblasts in cell culture. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGF. The function of EGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM_005860) is another VGAM200 host target gene. FSTL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FSTL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of FSTL3 BINDING SITE, designated SEQ ID:12473, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12742] Another function of VGAM200 is therefore inhibition of Follistatin-like 3 (secreted glycoprotein) (FSTL3, Accession NM_005860), a gene which is a member of the follistatin-module-protein family. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FSTL3. The function of FSTL3 has been established by previous studies. Follistatin-like-3 (FSTL3) is a member of the follistatin-module protein family, which is composed of extracellular matrix-associated glycoproteins thought to act in a paracrine manner to bind morphogens or growth/differentiation factors and regulate their activity during development (Hayette et al., 1998). In addition to the t(11;19) translocation in a case of B-cell chronic lymphocytic leukemia from which FSTL3 was isolated, Hayette et al. (1998) also observed rearrangement of the FSTL3 gene in a case of B-cell non-Hodgkin lymphoma (NHL; 605027) and in a case of B-cell mantle zone lymphoma, suggesting that FSTL3 may be involved in the leukemogenesis process.

[12743] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12744] Hayette, S.; Gadoux, M.; Martel, S.; Bertrand, S.; Tigaud, I.; Magaud, J.-P.; Rimokh, R. : FLRG (follistatin-related gene), a new target of chromosomal rearrangement in malignant blood disorders. *Oncogene* 16: 2949–2954, 1998. ; and

[12745] Rimokh, R.; Berger, F.; Delsol, G.; Charrin, C.; Bertheas, M. F.; Ffrench, M.; Garoscio, M.; Felman, P.; Coiffier, C.; Bryon, P. A. : Rearrangement and overexpression of the BCL-1/PRAD-1.

[12746] Further studies establishing the function and utilities of FSTL3 are found in John Hopkins OMIM database record ID 605343, and in cited publications numbered 4423, 545 and 4906 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 1 Receptor Antagonist (IL1RN, Accession NM_000577) is another VGAM200 host target gene. IL1RN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IL1RN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

IL1RN BINDING SITE, designated SEQ ID:6179, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12747] Another function of VGAM200 is therefore inhibition of Interleukin 1 Receptor Antagonist (IL1RN, Accession NM_000577), a gene which inhibits the activity of il-1 by binding to its receptor. il-1ra has no il-1 like activity. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RN. The function of IL1RN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM193. Insulin Receptor (INSR, Accession XM_048346) is another VGAM200 host target gene. INSR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by INSR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of INSR BINDING SITE, designated SEQ ID:35154, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12748] Another function of VGAM200 is therefore inhibition of Insulin Receptor (INSR, Accession XM_048346), a gene which binds insulin and has a tyrosine–protein kinase activity. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with INSR. The function of INSR has been established by previous studies. The insulin (INS; 176730) receptor is a tetramer of 2 alpha and 2 beta subunits. The alpha and beta subunits are coded by a single gene and are joined by disulfide bonds, a mechanism parallel to that of the ligand, insulin (Rubin, 1984). Mutation in either the structural gene or some of the processing steps may lead to insulin resistance. Ullrich et al. (1985) deduced the entire 1,370–amino acid sequence from a cDNA clone. The precursor starts with a 27–amino acid signal sequence, followed by the receptor alpha subunit, a precursor processing enzyme cleavage site, then the beta subunit containing a single 23–amino acid transmembrane sequence. Seino et al. (1989) found that the INSR gene spans more than 120 kb and has 22 exons. All introns interrupt protein coding regions of the gene. The 11 exons encoding the alpha subunit are dispersed over more than 90 kb, whereas the 11 exons encoding the beta subunit

are located together in a region of about 30 kb. Three transcriptional initiation sites were identified, located 276, 282, and 283 bp upstream of the translation initiation site. There is heterogeneity of insulin receptors in different tissues Leibiger et al. (2001) showed that insulin activates the transcription of its own gene and that of the beta-cell glucokinase gene (GCK; 138079) by different mechanisms. Whereas INS gene transcription is promoted by signaling through INSR type A (without exon 11), phosphatidylinositol 3-kinase (PI3K) class IA (see OMIM Ref. No. 171833), and the 70-kD S6 kinase, insulin stimulates the beta-cell GCK gene by signaling via INSR type B (with exon 11), PI3K class II (see OMIM Ref. No. 602838)-like activity, and protein kinase B (OMIM Ref. No. 164730). These data provided evidence for selectivity in insulin action via the 2 INSR isoforms, the molecular basis being preferential signaling through different PI3K and protein kinases. Using a yeast 2-hybrid system, Dey et al. (1998) identified a regulatory subunit of PI3K, PIK3R3 (OMIM Ref. No. 606076), as a binding partner of INSR. They concluded that PIK3R3 interacts with IGF1R (OMIM Ref. No. 147370) and INSR in a kinase-dependent manner, providing an alternative pathway for the activation of PI3K by

these 2 receptors. Rajala and Anderson (2001) sought to identify the tyrosine–phosphorylated protein(s) in the bovine rod outer segments (ROS) that are associated with PI3K. They concluded that tyrosine phosphorylation of the beta subunit of the insulin receptor is involved in the regulation of PI3K activity in the ROS. Animal model experiments lend further support to the function of INSR. Belke et al. (2002) generated mice with a cardiomyocyte–specific insulin receptor knockout (CIRKO), using cre/loxP recombination. Hearts of CIRKO mice were 20 to 30% smaller because of decreased postnatal hypertrophy of cardiomyocytes; they had persistent expression of the fetal beta–myosin heavy chain isoform, approximately half the normal expression of glucose transporter–1 (GLUT1; 138140), and a 2–fold increase in GLUT4 expression. Cardiac glucose uptake was increased in vivo, glycolysis was increased in isolated working hearts, and there was reduced expression of enzymes that catalyze mitochondrial beta–oxidation, leading to decreased fatty acid oxidation rates.

[12749] It is appreciated that the abovementioned animal model for INSR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appre–

ciated from the publications sited hereinbelow.

[12750] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12751] Leibiger, B.; Leibiger, I. B.; Moede, T.; Kemper, S.; Kulkarni, R. N.; Kahn, C. R.; de Vargas, L. M.; Berggren, P.-O. : Selective insulin signaling through A and B insulin receptors regulates transcription of insulin and glucokinase genes in pancreatic beta cells. *Molec. Cell* 7: 559–570, 2001. ; and

[12752] Belke, D. D.; Betuing, S.; Tuttle, M. J.; Gravelleau, C.; Young, M. E.; Pham, M.; Zhang, D.; Cooksey, R. C.; McClain, D. A.; Litwin, S. E.; Taegtmeyer, H.; Severson, D.; Kahn, C. R.; Abe.

[12753] Further studies establishing the function and utilities of INSR are found in John Hopkins OMIM database record ID 147670, and in sited publications numbered 129, 11700–11706, 11709–11708, 11710–11711, 3941–3945, 11278–3967, 11442–11443, 1210, 2612–2639, 12698, 3190, 3192–319 and 4710–3209 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Integrin, Alpha L (antigen CD11A (p180), Lymphocyte Function-associated

Antigen 1; Alpha Polypeptide) (ITGAL, Accession NM_002209) is another VGAM200 host target gene. ITGAL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGAL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGAL BINDING SITE, designated SEQ ID:7973, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12754] Another function of VGAM200 is therefore inhibition of Integrin, Alpha L (antigen CD11A (p180), Lymphocyte Function-associated Antigen 1; Alpha Polypeptide) (ITGAL, Accession NM_002209), a gene which is a receptor for icam1, icam2, icam3 and icam4. It is involved in a variety of immune phenomena including leukocyte-endothelial cell interaction, cytotoxic t-cell mediated killing, and antibody dependent killing by granulocytes and monocytes. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGAL. The function of ITGAL has been established by previous studies. See 120980 and 151510. Lymphocyte function-associated antigen-1 (LFA-1) shares

a beta subunit (see OMIM Ref. No. 116920) with other members of a family of leukocyte surface membrane antigens but has a unique alpha subunit (Sanchez-Madrid et al., 1983). LFA-1 is expressed on lymphocytes and phagocytic cells. The LFA-1 molecule is involved in the adhesion of cytotoxic T cells to their target cells. Patients with LFA-1 immunodeficiency disease (see OMIM Ref. No. 116920) have recurrent life-threatening infections, show deficiency of the beta chain of all 3 molecules, LFA-1, Mac-1 (macrophage antigen-1), and p150,95, and display profound defects in adhesion-dependent granulocyte, monocyte, and B- and T-lymphocyte functions. The alpha subunits were designated by Marlin et al. (1986) as alpha-L for LFA-1, alpha-M for Mac-1, and alpha-X for p150,95. Lu and Cyster (2002) studied the mechanisms that control localization of marginal zone B cells. They demonstrated that marginal zone B cells express elevated levels of the integrins LFA-1 and alpha-4-beta-1 (see OMIM Ref. No. 192975 and 135630) and that the marginal zone B cells bind to the ligands ICAM1 (OMIM Ref. No. 147840) and VCAM1 (OMIM Ref. No. 192225). These ligands are expressed within the marginal zone in a lymphotoxin-dependent manner. Combined inhibition of LFA-1 and alpha-

4-beta-1 causes a rapid and selective release of B cells from the marginal zone. Furthermore, lipopolysaccharide-triggered marginal zone B cell relocalization involves down-regulation of integrin-mediated adhesion. Lu and Cyster (2002) concluded that their studies identified key requirements for marginal zone B cell localization and established a role for integrins in peripheral lymphoid tissue compartmentalization

[12755] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12756] Lu, T. T.; Cyster, J. G. : Integrin-mediated long-term B cell retention in the splenic marginal zone. Science 297: 409-412, 2002. ; and

[12757] Marlin, S. D.; Morton, C. C.; Anderson, D. C.; Springer, T. A. : LFA-1 immunodeficiency disease: definition of the genetic defect and chromosomal mapping of alpha and beta subunits of t.

[12758] Further studies establishing the function and utilities of ITGAL are found in John Hopkins OMIM database record ID 153370, and in cited publications numbered 4962, 4964, 3348, 354 and 3556 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Jagged 2 (JAG2, Accession NM_002226) is another VGAM200 host target gene. JAG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAG2 BINDING SITE, designated SEQ ID:8006, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12759] Another function of VGAM200 is therefore inhibition of Jagged 2 (JAG2, Accession NM_002226), a gene which is a putative notch ligand involved in the mediation of notch signaling. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAG2. The function of JAG2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM136. Junctional Adhesion Molecule 3 (JAM3, Accession NM_032801) is another VGAM200 host target gene. JAM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAM3,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM3 BINDING SITE, designated SEQ ID:26553, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12760] Another function of VGAM200 is therefore inhibition of Junctional Adhesion Molecule 3 (JAM3, Accession NM_032801), a gene which is a member of the junctional adhesion molecule protein family. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM3. The function of JAM3 has been established by previous studies. JAM3 is a member of the junctional adhesion molecule (JAM) family. The first identified member of the JAM family, JAM1 (OMIM Ref. No. 605721), is an immunoglobulin (Ig)-like molecule that colocalizes with tight junctions in endothelium and epithelium and is also found on blood leukocytes and platelets. Adhesion proteins targeted to cell-cell borders, like JAM1, are ideally situated to participate in leukocyte emigration. By searching an EST database for sequences similar to JAM2 (OMIM Ref. No. 606870), followed by amplification of a fetal brain cDNA library, Ar-

rate et al. (2001) isolated a cDNA encoding JAM3. The deduced 310-amino acid protein is more than 30% identical to JAM2 and JAM1. It possesses a signal sequence; 2 Ig-like folds, one a V type and the other a C2 type, containing 6 cysteines; 2 potential N-glycosylation sites; and a 46-amino acid intracellular tail with a C-terminal binding motif for PDZ domains and a phosphorylation site. Northern blot analysis revealed wide expression of an approximately 3.3-kb transcript, with highest levels in placenta, brain, and kidney. Expression was also detected in cultured endothelial cells. Binding analysis showed that unlike JAM2, JAM3 is unable to adhere to leukocyte cell lines and only forms weak homotypic interactions. However, JAM3 was found to interact strongly with JAM2. RT-PCR and flow cytometric analyses detected strong expression in cytotoxic T-cell lines and activated T lymphocytes, but not in resting cells. Immunoprecipitation analysis indicated that the 43-kD JAM3 protein binds with JAM2. While studying JAM2 with immunoprecipitation analysis, Liang et al. (2002) identified a 40-kD protein and subsequently cloned JAM3. Western blot analysis showed expression on natural killer cells. Liang et al. (2002) proposed that JAM3 is a functional JAM2 receptor.

[12761] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12762] Arrate, M. P.; Rodriguez, J. M.; Tran, T. T.; Brock, T. A.; Cunningham, S. A. : Cloning of human junctional adhesion molecule 3 (JAM3) and its identification as the JAM2 counter-receptor. J. Biol. Chem. 276: 45826–45832, 2001. ; and

[12763] Liang, T. W.; Chiu, H. H.; Gurney, A.; Sidle, A.; Tumas, D. B.; Schow, P.; Foster, J.; Klassen, T.; Dennis, K.; DeMarco, R. A.; Pham, T.; Frantz, G.; Fong, S. : Vascular endothelial-jun.

[12764] Further studies establishing the function and utilities of JAM3 are found in John Hopkins OMIM database record ID 606871, and in cited publications numbered 5392 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269) is another VGAM200 host target gene. LEF1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LEF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of LEF1 BINDING SITE, designated SEQ ID:18392, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12765] Another function of VGAM200 is therefore inhibition of Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269), a gene which plays an essential role in the formation of several organs and structures that require inductive tissue interactions. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEF1. The function of LEF1 has been established by previous studies. Lymphoid enhancer-binding factor-1 (LEF1) is a 48-kD nuclear protein that is expressed in pre-B and T cells. It binds to a functionally important site in the T-cell receptor-alpha (TCRA; 186880) enhancer and confers maximal enhancer activity. LEF1 belongs to a family of regulatory proteins that share homology with high mobility group protein-1 (HMG1; 163905). Animal model experiments lend further support to the function of LEF1. Lef1 is a sequence-specific DNA-binding protein that is expressed in pre-B and T lymphocytes of adult mice, and in the neural crest, mesencephalon, tooth germs, whisker follicles, and

other sites during mouse embryogenesis. Van Genderen et al. (1994) generated mice carrying a homozygous germline mutation in the Lef1 gene that eliminated Lef1 protein expression and caused postnatal lethality. The mutant mice lacked teeth, mammary glands, whiskers, and hair, although they developed rudimentary hair follicles. The Lef1-deficient mice also lacked the mesencephalic nucleus of the trigeminal nerve, the only neural crest-derived neuronal populations. The mutant mice showed no obvious defects in lymphoid cell populations at birth. Van Genderen et al. (1994) suggested that Lef1 plays an essential role in the formation of several organs and structures that require inductive tissue interactions

[12766] It is appreciated that the abovementioned animal model for LEF1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12767] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12768] van Genderen, C.; Okamura, R. M.; Farinas, I.; Quo, R. G.; Parslow, T. G.; Bruhn, L.; Grosschedl, R. : Development of several organs that require inductive epithelial-mes-

enchymal interactions is impaired in LEF-1-deficient mice.

Genes Dev. 8: 2691-2703, 1994. ; and

[12769] de Lau, W.; Clevers, H. : LEF1 turns over a new leaf. Nature Genet. 28: 3-5, 2001.

[12770] Further studies establishing the function and utilities of LEF1 are found in John Hopkins OMIM database record ID 153245, and in cited publications numbered 11514-11521 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Myosin IE (MYO1E, Accession NM_004998) is another VGAM200 host target gene. MYO1E BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MYO1E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1E BINDING SITE, designated SEQ ID:11442, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12771] Another function of VGAM200 is therefore inhibition of Myosin IE (MYO1E, Accession NM_004998), a gene which is an unconventional myosin. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with MYO1E. The function of MYO1E has been established by previous studies. Bement et al. (1994) cloned a human unconventional myosin gene, MYO1E, encoding a predicted 127-kD polypeptide of 1,109 amino acids. The gene, which they designated myosin IC, contains a characteristic N-terminal myosin head, a single 'IQ motif' predicted to bind a single myosin light chain, and a C-terminal tail with a putative membrane-binding site. They also noted the presence of a C-terminal src-homology domain, reminiscent of 'long-tailed' myosins I from amoeboid organisms. By Northern analysis, Bement et al. (1994) detected ubiquitous expression of MYO1E. Hasson et al. (1996) used fluorescence in situ hybridization to map the loci for 4 unconventional myosin loci in humans: MYO1E (formerly MYO1C), MYO1A (OMIM Ref. No. 601478), MYO1F (OMIM Ref. No. 601480), and MYO10 (OMIM Ref. No. 601481). The MYO1E gene was found to be located on 15q21-q22 in the precise location predicted from its location on chromosome 9 of the mouse.

[12772] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [12773] Bement, W. M.; Wirth, J. A.; Mooseker, M. S. : Cloning and mRNA expression of human unconventional myosin-IC: a homologue of amoeboid myosins-I with a single IQ motif and an SH3 domain. J. Molec. Biol. 243: 356-363, 1994. ; and
- [12774] Hasson, T.; Skowron, J. F.; Gilbert, D. J.; Avraham, K. B.; Perry, W. L.; Bement, W. M.; Anderson, B. L.; Sherr, E. H.; Chen, Z.-Y.; Greene, L. A.; Ward, D. C.; Corey, D. P.; Mooseker.
- [12775] Further studies establishing the function and utilities of MYO1E are found in John Hopkins OMIM database record ID 601479, and in cited publications numbered 651 and 7027 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531) is another VGAM200 host target gene. NTSR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NTSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTSR1 BINDING SITE, designated SEQ ID:8372, to the nucleotide sequence of VGAM200 RNA, herein designated

VGAM RNA, also designated SEQ ID:2911.

[12776] Another function of VGAM200 is therefore inhibition of Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531), a gene which is associated with g proteins that activate a phosphatidylinositol– calcium second messenger system. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTSR1. The function of NTSR1 has been established by previous studies. The tridecapeptide neurotensin (OMIM Ref. No. 162650) is widely distributed in various regions of the brain and in peripheral tissues. In the brain, neurotensin acts as a neuromodulator, in particular of dopamine transmission in the nigrostriatal and mesocorticolimbic systems, suggesting its possible implication in dopamine-associated behavioral neurodegenerative and neuropsychiatric disorders. Its various effects are mediated by specific membrane receptors. Vita et al. (1993) isolated a cDNA encoding a human neurotensin receptor (NTSR1) and showed that it predicts a 418–amino acid protein that shares 84% homology with the rat protein. Le et al. (1997) also cloned human NTSR1 cDNA and its genomic DNA. The gene contains 4 exons and spans more than 10 kb. The authors

identified a highly polymorphic tetranucleotide repeat approximately 3 kb from the gene. Southern blot analysis revealed that the NTSR1 gene is present in the human genome as a single-copy gene. Le et al. (1997) stated that the neurotensin receptor has 7 transmembrane spanning regions and high homology to other receptors that couple to G proteins. Vincent (1995) reviewed pharmacologic and molecular data suggesting the existence of other types of functional neurotensin receptors.

[12777] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12778] Le, F.; Groshan, K.; Zeng, X. P.; Richelson, E. : Characterization of the genomic structure, promoter region, and a tetranucleotide repeat polymorphism of the human neurotensin receptor gene. J. Biol. Chem. 272: 1315–1322, 1997. ; and

[12779] Vincent, J.–P. : Neurotensin receptors: binding properties, transduction pathways, and structure. Cell. Molec. Neurobiol. 15: 501–512, 1995.

[12780] Further studies establishing the function and utilities of NTSR1 are found in John Hopkins OMIM database record ID 162651, and in cited publications numbered

5197–5200 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430) is another VGAM200 host target gene. PAFAH1B1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PAFAH1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAFAH1B1 BINDING SITE, designated SEQ ID:6013, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12781] Another function of VGAM200 is therefore inhibition of Platelet-activating Factor Acetylhydrolase, Isoform Ib, Alpha Subunit 45kDa (PAFAH1B1, Accession NM_000430). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAFAH1B1. Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession NM_002612) is another VGAM200 host target gene. PDK4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated

region of mRNA encoded by PDK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK4 BINDING SITE, designated SEQ ID:8477, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12782] Another function of VGAM200 is therefore inhibition of Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession NM_002612). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK4. Phosphatidylinositol 4-kinase, Catalytic, Beta Polypeptide (PIK4CB, Accession NM_002651) is another VGAM200 host target gene. PIK4CB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK4CB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK4CB BINDING SITE, designated SEQ ID:8513, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12783] Another function of VGAM200 is therefore inhibition of Phosphatidylinositol 4-kinase, Catalytic, Beta Polypeptide (PIK4CB, Accession NM_002651), a gene which phosphorylates the 4-OH position of phosphatidyl inositol. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK4CB. The function of PIK4CB has been established by previous studies. By degenerate PCR, library screening, and 5-prime-RACE, Meyers and Cantley (1997) cloned human placenta and heart cDNAs encoding a novel PI 4-kinase, which they called PI4K-beta. The predicted 801-amino acid PI4K-beta protein contains an N-terminal lipid kinase unique domain, which is shared by members of both the PI 3-kinase (e.g., 171834) and PI 4-kinase families, and a C-terminal catalytic domain, which defines this protein as a member of a much larger protein/lipid kinase family. PI4K-beta shares significant amino acid sequence similarity with yeast PIK1. Western blot analysis of mammalian cell lysates using an antibody against PI4K-beta detected a 110-kD protein. Northern blot analysis showed that PI4K-beta is ubiquitously expressed as an approximately 4-kb transcript, with highest expression in heart, pancreas, and skeletal muscle. Biochemical anal-

yses indicated that PI4K-beta is a type III enzyme that is sensitive to wortmannin. Meyers and Cantley (1997) stated that PI4K-beta is likely the wortmannin-sensitive PI 4-kinase described by Nakanishi et al. (1995) that is responsible for regulating the synthesis of agonist-sensitive pools of polyphosphoinositides. Saito et al. (1997) isolated a PI 4-kinase cDNA from a human adult brain cDNA library. The sequence of the cDNA was highly identical to that of the PI4K-beta cDNA (Meyers and Cantley, 1997), and Saito et al. (1997) suggested that they represented alternative products of the same gene. Suzuki et al. (1997) cloned 3 forms of cDNAs encoding human PIK4CB, which they named NPIK for 'novel putative phosphatidylinositol kinase;' 2 of the cDNAs had different 5-prime open reading frame sequences, and the third contained a 45-bp insertion within the coding sequence. The authors suggested that these cDNAs resulted from alternative transcription initiation sites and alternative splicing. By Northern blot analysis, they detected 4.8- and 3.6-kb transcripts whose relative levels varied in different tissues. Using the green fluorescent protein system, they demonstrated that PIK4CB is localized in the cytoplasm.

[12784] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [12785] Saito, T.; Seki, N.; Ishii, H.; Ohira, M.; Hayashi, A.; Kozuma, S.; Hori, T. : Complementary DNA cloning and chromosomal mapping of a novel phosphatidylinositol kinase gene. DNA Res. 4: 301–305, 1997. ; and
- [12786] Suzuki, K.; Hirano, H.; Okutomi, K.; Suzuki, M.; Kuga, Y.; Fujiwara, T.; Kanemoto, N.; Isono, K.; Horie, M. : Identification and characterization of a novel human phosphatidylinositol 4.
- [12787] Further studies establishing the function and utilities of PIK4CB are found in John Hopkins OMIM database record ID 602758, and in cited publications numbered 5889–5892 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pleckstrin (PLEK, Accession NM_002664) is another VGAM200 host target gene. PLEK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLEK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLEK BINDING SITE, designated SEQ ID:8533, to the nucleotide sequence of VGAM200 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2911.

[12788] Another function of VGAM200 is therefore inhibition of Pleckstrin (PLEK, Accession NM_002664), a gene which is the major protein kinase c substrate of platelets. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLEK. The function of PLEK has been established by previous studies. In platelets, agonists that stimulate phosphoinositide turnover cause the rapid phosphorylation of a protein of apparent relative molecular mass 40,000–47,000, called P47, by protein kinase C. Tyers et al. (1988) isolated human P47 clones by immunologic screening of a lambda-gt11 cDNA library from a promyelocytic leukemia cell line. A 1,050 basepair open reading frame that could encode the protein in question was confirmed by comparison with peptide sequences from platelet P47 and by expression of the putative P47 in *E. coli* and in vitro. The P47 sequence appeared to have been conserved throughout vertebrate evolution and was not similar to any other known sequence, including lipocortin (OMIM Ref. No. 151690). Based on its specific expression in platelets and various differentiated white blood cells, Tyers et al. (1988) proposed the name pleckstrin for

platelet and leukocyte C kinase substrate and for the KSTR string of amino acids in the sequence KFARKSTRRSIR, the probable phosphorylation site. Tyers et al. (1989) re-reported the pleckstrin sequence. They deduced a molecular weight of 40,087. By differential display comparison of murine epidermal promotion-sensitive and -resistant cell lines after exposure to a tumor promoter, phorbol ester TPA, Cmarik et al. (2000) observed preferential expression in promotion-resistant cells of a cDNA encoding Plek. Northern blot analysis detected a 3.6-kb Plek transcript in mouse heart, lung, and spleen. Mouse Plek shares 91% amino acid identity with human PLEK. Using an interspecific backcross panel, Cmarik et al. (2000) mapped the mouse Plek gene to the proximal part of chromosome 11 in a region showing homology of synteny to human 2p, where they stated the PLEK gene has been mapped.

[12789] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12790] Cmarik, J. L.; Hegamyer, G.; Gerrard, B.; Dean, M.; Colburn, N. H. : cDNA cloning and mapping of mouse pleckstrin (Plek), a gene upregulated in transformation-resistant cells. *Genomics* 66: 204-212, 2000. ; and

[12791] Tyers, M.; Haslam, R. J.; Rachubinski, R. A.; Harley, C. B. : Molecular analysis of pleckstrin: the major protein kinase C substrate of platelets. J. Cell. Biochem. 40: 133–145, 1989.

[12792] Further studies establishing the function and utilities of PLEK are found in John Hopkins OMIM database record ID 173570, and in cited publications numbered 1195–1197 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Parathymosin (PTMS, Accession NM_002824) is another VGAM200 host target gene. PTMS BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTMS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTMS BINDING SITE, designated SEQ ID:8696, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12793] Another function of VGAM200 is therefore inhibition of Parathymosin (PTMS, Accession NM_002824), a gene which is involved in the regulation of cellular immunity. Accordingly, utilities of VGAM200 include diagnosis, pre–

vention and treatment of diseases and clinical conditions associated with PTMS. The function of PTMS has been established by previous studies. Parathymosin is a polypeptide similar in size and amino acid composition to prothymosin- α (OMIM Ref. No. 188390). It has a high content of dicarboxylic amino acids and a complete absence of aromatic and sulfur-containing amino acids. It has 101 amino acid residues as compared to 111 for prothymosin. Clinton et al. (1989) reported the isolation of a cDNA clone for human kidney parathymosin containing the complete coding region and extending into the 5-prime and 3-prime flanking sequences. The open reading frame contains 306 nucleotides, including the codon for the initiator methionine. Analysis of the 5-prime flanking sequence excluded the presence of a hydrophobic signal peptide in the translated sequence. This permitted the conclusion that parathymosin, like prothymosin- α , is synthesized without formation of a larger precursor polypeptide. Parathymosin and prothymosin show a reciprocal relationship: the highest levels of parathymosin and its mRNA are present in liver, kidney, and brain (with lowest levels in thymus and spleen), whereas prothymosin- α and its mRNA are present in highest concentrations in

thymus and spleen (with lower levels in kidney, brain, and liver). By in situ hybridization of rat parathymosin cDNA to human metaphase chromosomes, Szabo et al. (1989) localized the gene for human parathymosin to 17q12-q22.

[12794] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12795] Clinton, M.; Frangou-Lazaridis, M.; Panneerselvam, C.; Horecker, B. L. : The sequence of human parathymosin deduced from a cloned human kidney cDNA. Biochem. Biophys. Res. Commun. 158: 855-862, 1989. ; and

[12796] Szabo, P.; Clinton, M.; Macera, M.; Horecker, B. L. : Localization of the gene coding for parathymosin to chromosome 17 in humans. Cytogenet. Cell Genet. 50: 91-92, 1989.

[12797] Further studies establishing the function and utilities of PTMS are found in John Hopkins OMIM database record ID 168440, and in cited publications numbered 2387-2388 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAS Guanyl Releasing Protein 1 (calcium and DAG-regulated) (RASGRP1, Accession NM_005739) is another VGAM200 host target gene. RASGRP1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by RASGRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASGRP1 BINDING SITE, designated SEQ ID:12303, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12798] Another function of VGAM200 is therefore inhibition of RAS Guanyl Releasing Protein 1 (calcium and DAG-regulated) (RASGRP1, Accession NM_005739). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRP1. Regenerating Islet-derived-like, Pancreatic Stone Protein-like, Pancreatic Thread Protein-like (rat) (REGL, Accession NM_006508) is another VGAM200 host target gene. REGL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by REGL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of REGL BINDING SITE, designated SEQ ID:13257, to the nucleotide sequence of VGAM200

RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12799] Another function of VGAM200 is therefore inhibition of Regenerating Islet–derived–like, Pancreatic Stone Protein–like, Pancreatic Thread Protein–like (rat) (REGL, Accession NM_006508), a gene which is a member of REG family with unknown function. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with REGL. The function of REGL has been established by previous studies. The REG1A (OMIM Ref. No. 167770) and REG1B genes belong to the type I subclass of the REG family of genes, each of which encodes a 166–amino acid protein. Moriizumi et al. (1994) and Gharib et al. (1993) mapped the REG1A and REG1B genes to 2p12. Miyashita et al. (1995) demonstrated that 4 REG family genes are tandemly ordered in a 95–kb DNA region of 2p12. From analysis of YAC clones containing the 4 genes using 2–color fluorescence in situ hybridization, they demonstrated the following order: 2cen--PAP--RS--REG1A--REG1B--ptel. (RS, so designated for REG–related sequence, shows a high degree of homology to the REG1 genes but has an in–frame stop codon in the protein coding region.)

[12800] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12801] Miyashita, H.; Nakagawara, K.; Mori, M.; Narushima, Y.; Noguchi, N.; Moriizumi, S.; Takasawa, S.; Yonekura, H.; Takeuchi, T.; Okamoto, H. : Human REG family genes are tandemly ordered in a 95-kilobase region of chromosome 2p12. FEBS Lett. 377: 429–433, 1995. ; and

[12802] Moriizumi, S.; Watanabe, T.; Unno, M.; Nakagawara, K.; Suzuki, Y.; Miyashita, H.; Yonekura, H.; Okamoto, H. : Iso-lation, structural determination and expression of a novel reg gene, hum.

[12803] Further studies establishing the function and utilities of REGL are found in John Hopkins OMIM database record ID 167771, and in cited publications numbered 10915, 1091 and 10925 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Selectin P Ligand (SELPLG, Accession XM_006867) is another VGAM200 host target gene. SELPLG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SELPLG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of SELPLG BINDING SITE, designated SEQ ID:30020, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12804] Another function of VGAM200 is therefore inhibition of Selectin P Ligand (SELPLG, Accession XM_006867), a gene which binds to p-, e- and l-selectins, which mediates the tethering and rolling of neutrophils and t-lymphocytes on endothelial cells. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SELPLG. The function of SELPLG has been established by previous studies. Human granulocyte ehrlichiosis (HGE) is a febrile tick-bone illness caused by an intracellular bacterium remarkable for its tropism for professionally phagocytic neutrophils. Herron et al. (2000) demonstrated that monoclonal antibodies against the P-selectin binding domain of the leukocyte P-selectin glycoprotein ligand PSGL1 prevented HGE cell binding and infection, as did enzymatic digestion of PSGL1. Furthermore, simultaneous neoexpression in non-susceptible cells of complementary DNAs for both PSGL1 and its modifying alpha-(1,3) fucosyltransferase, Fuc-TVII (FUT7), allowed binding and infection by HGE. Thus, the

HGE bacterium specifically bound to fucosylated leukocyte PSGL1. Selection mimicry is likely central to the organism's unique ability to target and infect neutrophils. Selectin P ligand, or P-selectin glycoprotein ligand (OMIM Ref. No. PSGL-1), is the high affinity counter-receptor for P-selectin (SELP; 173610) on myeloid cells and stimulated T lymphocytes. As such, it plays a critical role in the tethering of these cells to activated platelets or endothelia expressing P-selectin. Veldman et al. (1995) cloned the SELPLG gene from a human placenta genomic DNA library and showed that a single intron of approximately 9 kb is located in the 5-prime untranslated region and that the complete coding region resides in exon 2. The organization of the gene, designated SELPLG, closely resembles that of CD43 (OMIM Ref. No. 182160) and the human platelet glycoprotein Gplb-alpha (OMIM Ref. No. 231200), both of which have an intron in the 5-prime-noncoding region, a long second exon containing the complete coding region, and TATA-less promoters.

[12805] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12806] Herron, M. J.; Nelson, C. M.; Larson, J.; Snapp, K. R.;

Kansas, G. S.; Goodman, J. L. : Intracellular parasitism by the human granulocytic ehrlichiosis bacterium through the P-selectin ligand, PSGL-1. Science 288: 1653-1656, 2000. ; and

[12807] Veldman, G. M.; Bean, K. M.; Cumming, D. A.; Eddy, R. L.; Sait, S. N. J.; Shows, T. B. : Genomic organization and chromosomal localization of the gene encoding human P-selectin glycop.

[12808] Further studies establishing the function and utilities of SELPLG are found in John Hopkins OMIM database record ID 600738, and in cited publications numbered 7575-7578 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598) is another VGAM200 host target gene. SLC12A7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC12A7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A7 BINDING SITE, designated SEQ ID:13375, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM

RNA, also designated SEQ ID:2911.

[12809] Another function of VGAM200 is therefore inhibition of Solute Carrier Family 12 (potassium/chloride transporters), Member 7 (SLC12A7, Accession NM_006598), a gene which is a potassium/chloride-cotransporter. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A7. The function of SLC12A7 has been established by previous studies. By searching EST databases, Mount et al. (1999) identified a cDNA encoding SLC12A7, which they initially termed KCC3 but later renamed KCC4. The deduced 1,083-amino acid SLC12A7 protein contains 12 membrane-spanning segments, 8 phosphorylation sites, 7 of which are in the C terminus, and 4 potential N-glycosylation sites. SLC12A7 shares 65% amino acid identity with SLC12A4 (OMIM Ref. No. 604119) and 66% identity with SLC12A6 (OMIM Ref. No. 604878). Northern blot analysis detected a 5.3-kb SLC12A7 transcript in most tissues tested, with highest expression in heart and kidney and little or no expression in adult brain. Functional analysis confirmed that SLC12A7 is a KCC. Animal model experiments lend further support to the function of SLC12A7. Boettger et al. (2002) gener-

ated mice constitutively lacking KCC4, which is predominantly expressed in kidney, heart, lung, and liver. *Kcc4* $-/-$ mice were born at the expected mendelian ratio. They were viable and fertile; however, their body weight was roughly 90% that of their littermates. Mice had normal hearing loss at postnatal day 14, indicated by normal auditory brainstem responses. Hearing deteriorated quickly during the following week, after which mice were nearly deaf, with a hearing loss of 70 to 80 decibels. Histologic analysis revealed that the inner ear developed normally and could not be distinguished from those of wildtype animals at postnatal day 14. At postnatal day 21, however, outer hair cells of basal turns of the cochlea were almost totally absent, whereas inner hair cells were still present. The degeneration proceeded from basal to apical turns. In adult knockout mice, the organ of Corti was lost completely in basal turns. In apical turns, some hair cells survived, accounting for the residual hearing ability in adult mice. Even in adult mice, there was no collapse of the Reissner membrane, which separates the scala media from the scala vestibuli, suggesting that *Kcc4* is not essential for endolymph production. Outer hair cells of *Kcc4* $-/-$ mice degenerated before Deiters cells were lost, although

Deiters cells and not outer hair cells normally express Kcc4 at this stage. This is consistent with a disturbance of extracellular homeostasis due to impaired salt uptake by Deiters cells, and may lead to death of outer hair cells by osmotic stress or membrane depolarization. Deafness in Kcc4 $-/-$ mice was associated with renal tubular acidosis. The urine of knockout mice was more alkaline than that of wildtype littermates, whereas concentrations of sodium, potassium, and chloride were not changed. Blood gas analysis indicated a compensated metabolic acidosis with significantly decreased base excess. Immunofluorescence revealed that Kcc4 is expressed in basolateral membranes of several nephron segments. Intracellular chloride concentration was increased in proximal tubules and particularly in alpha-intercalated cells of knockout mice. Considering the prominent chloride/bicarbonate exchange activity in alpha-intercalated cells, the rise in intracellular chloride predicts a more alkaline intracellular pH in the knockout mice. This will decrease apical proton secretion by increasing the electrochemical gradient against which pumping has to occur. Thus, KCC4 joins the hydrogen ATPase (OMIM Ref. No. 192132) and AE1 anion exchanger (OMIM Ref. No. 109270) as the third transport protein of

alpha-intercalated cells whose mutation entails renal tubular acidosis. Boettger et al. (2002) concluded that KCC4 is important for potassium recycling by siphoning potassium ions after their exit from outer hair cells into supporting Deiters cells, where potassium enters the gap junction pathway.

[12810] It is appreciated that the abovementioned animal model for SLC12A7 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[12811] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12812] Mount, D. B.; Mercado, A.; Song, L.; Xu, J.; George, A. L., Jr.; Delpire, E.; Gamba, G. : Cloning and characterization of KCC3 and KCC4, new members of the cation-chloride cotransporter gene family. J. Biol. Chem. 274: 16355–16362, 1999. ; and

[12813] Boettger, T.; Hubner, C. A.; Maler, H.; Rust, M. B.; Beck, F. X.; Jentsch, T. J. : Deafness and renal tubular acidosis in mice lacking the K-Cl co-transporter Kcc4. Nature 416: 874–878, 20.

[12814] Further studies establishing the function and utilities of

SLC12A7 are found in John Hopkins OMIM database record ID 604879, and in cited publications numbered 6944 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 38, Member 2 (SLC38A2, Accession NM_018976) is another VGAM200 host target gene. SLC38A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC38A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC38A2 BINDING SITE, designated SEQ ID:21049, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12815] Another function of VGAM200 is therefore inhibition of Solute Carrier Family 38, Member 2 (SLC38A2, Accession NM_018976), a gene which is an amino acid transporter. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC38A2. The function of SLC38A2 has been established by previous studies. . Sugawara et al. (2000) cloned a rat skeletal muscle Ata2 cDNA. The deduced Ata2 protein shares 55% sequence identity with the

rat glutamine transporter GlnT (Ata1). When expressed in mammalian cells, Ata2 mediated sodium-dependent transport of MeAIB. The Ata2 transporter was specific for neutral amino acids. It was pH-sensitive and lithium-intolerant. The sodium:amino acid stoichiometry was 1:1. When expressed in *Xenopus* oocytes, transport of neutral amino acids via Ata2 was associated with inward currents. The substrate-induced current was sodium-dependent and pH-sensitive. By screening human fetal brain cDNAs for the potential to encode large proteins, Nagase et al. (2000) isolated a partial ATA2 cDNA, which they called KIAA1382, that lacks 5-prime coding sequence. The deduced 462-amino acid ATA2 partial protein shares 57% amino acid sequence identity with the human transporter protein g17 across 98% of its length. RT-PCR followed by ELISA detected ATA2 expression in all human tissues examined, with the highest level in adult brain. Within the brain, ATA2 expression was found in all regions tested, with the highest level in the subthalamic nucleus.

[12816] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12817] Nagase, T.; Kikuno, R.; Ishikawa, K.; Hirosawa, M.; Ohara,

O. : Prediction of the coding sequences of unidentified human genes. XVI. The complete sequences of 150 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 7: 65–73, 2000. ; and

[12818] Sugawara, M.; Nakanishi, T.; Fei, Y.-J.; Huang, W.; Ganapathy, M. E.; Leibach, F. H.; Ganapathy, V. : Cloning of an amino acid transporter with functional characteristics and tissue exp.

[12819] Further studies establishing the function and utilities of SLC38A2 are found in John Hopkins OMIM database record ID 605180, and in cited publications numbered 6371 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Synaptogyrin 1 (SYNGR1, Accession NM_004711) is another VGAM200 host target gene. SYNGR1 BINDING SITE1 and SYNGR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SYNGR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNGR1 BINDING SITE1 and SYNGR1 BINDING SITE2, designated SEQ ID:11060 and SEQ ID:11068 respectively, to the nucleotide sequence of VGAM200 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2911.

[12820] Another function of VGAM200 is therefore inhibition of Synaptogyrin 1 (SYNGR1, Accession NM_004711), a gene which belongs to transmembrane synaptic vesicle protein and may function in membrane recycling. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNGR1. The function of SYNGR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM107. Tripartite Motif-containing 9 (TRIM9, Accession NM_052978) is another VGAM200 host target gene. TRIM9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM9 BINDING SITE, designated SEQ ID:27551, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12821] Another function of VGAM200 is therefore inhibition of Tripartite Motif-containing 9 (TRIM9, Accession

NM_052978), a gene which may function as a positive regulator for mannosylphosphate transferase and is required to mediate mannosylphosphate transfer in both the core and outer chain portions of n-linked oligosaccharides. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM9. The function of TRIM9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Transient Receptor Potential Cation Channel, Subfamily C, Member 1 (TRPC1, Accession NM_003304) is another VGAM200 host target gene. TRPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC1 BINDING SITE, designated SEQ ID:9305, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12822] Another function of VGAM200 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C,

Member 1 (TRPC1, Accession NM_003304), a gene which acts as a non-voltage-sensitive store-operated Ca^{2+} channel. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC1. The function of TRPC1 has been established by previous studies. Zitt et al. (1996) cloned a truncated TRPC1 cDNA, which they designated TRPC1A, that lacks amino acids 109–143 of the human TRP1 sequence. By transfection studies in Chinese hamster ovary cells, Zitt et al. (1996) showed that the TRPC1A gene product functions as a store-operated calcium-permeable cation channel. Zhu et al. (1996) similarly showed that TRPC1 increased store-operated calcium entry in transfected COS cells. Xu et al. (1997) reported that the TRPC1 and TRPC3 proteins form heteromultimeric complexes. Berg et al. (1997) stated that TRPC1 is expressed in megakaryocytic cell lines and therefore may play a role in calcium homeostasis in megakaryocytes and platelets.

[12823] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12824] Zitt, C.; Zobel, A.; Obukhov, A. G.; Harteneck, C.; Kalk-

brenner, F.; Luckhoff, A.; Schultz, G. : Cloning and functional expression of a human Ca(2+)-permeable cation channel activated by calcium store depletion. Neuron 16: 1189-1196, 1996. ; and

[12825] Xu, X.-Z. S.; Li, H.-S.; Guggino, W. B.; Montell, C. : Coassembly of TRP and TRPL produces a distinct store-operated conductance. Cell 89: 1155-1164, 1997.

[12826] Further studies establishing the function and utilities of TRPC1 are found in John Hopkins OMIM database record ID 602343, and in cited publications numbered 1007-1012 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_080706) is another VGAM200 host target gene. TRPV1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPV1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPV1 BINDING SITE, designated SEQ ID:28014, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12827] Another function of VGAM200 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily V, Member 1 (TRPV1, Accession NM_080706), a gene which functions as a receptor for capsaicin. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPV1. The function of TRPV1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM146. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM200 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28453, SEQ ID:28470 and SEQ ID:17189 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12828] Another function of VGAM200 is therefore inhibition of

Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 has been established by previous studies. Wolf–Hirschhorn syndrome (WHS; 194190) is a malformation syndrome associated with a hemizygous deletion of the distal short arm of chromosome 4 (OMIM Ref. No. 4p16.3). The shortest region of overlap of the deletions observed in WHS patients, the WHS critical region, has been confined to a region of 165 kb (Wright et al., 1997). This region was sequenced completely during the search for the Huntington disease gene (Baxendale et al., 1993). Stec et al. (1998) described a novel developmental gene, two-thirds of which maps in the distal part of the WHS critical region. They designated the gene WHSC1 (Wolf–Hirschhorn syndrome candidate–1). The WHSC1 gene was identified initially through its high similarity to the translation product of an expressed sequence tag, located in the 165–kb WHCR, with the SET domain (see OMIM Ref. No. 600960) of the *Drosophila* protein ASH1 (OMIM Ref. No. 100790). The SET domain is found in pro–

teins that are involved in embryonic development. The 25-exon WHSC1 gene was found to be expressed ubiquitously in early development and to undergo complex alternative splicing and differential polyadenylation. It encodes a 136-kD protein containing 4 domains present in other developmental proteins: a PWWP domain, an HMG box, a SET domain also found in the *Drosophila* dysmorph gene ash-encoded protein, and a PHD-type zinc finger. It is expressed preferentially in rapidly growing embryonic tissues, in a pattern corresponding to affected organs in WHS patients. The nature of the protein motifs, the expression pattern, and its mapping to the critical region led Stec et al. (1998) to propose WHSC1 as a good candidate gene to be responsible for many of the phenotypic features of WHS. Stec et al. (1998) noted that the t(4;14)(p16.3;q32.3) translocations described in a significant fraction of multiple myelomas (Richelda et al., 1997; Chesi et al., 1997) have breakpoints located less than 100 kb centromeric of the FGFR3 gene (OMIM Ref. No. 134934) on 4p16.3. They found that at least 3 of the breakpoints merged the immunoglobulin heavy-chain gene (IGHG1; 147100) on chromosome 14 with the WHSC1 gene. This fusion of genes and their untimely ex-

pression in the myeloid lineage driven from the 5-prime IgH enhancer may indicate that WHSC1-encoded proteins are involved in the clinical heterogeneity of multiple myeloma.

[12829] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12830] Chesi, M.; Nardini, E.; Brents, L. A.; Schrock, E.; Ried, T.; Kuehl, W. M.; Bergsagel, P. L. : Frequent translocation t(4;14)(p16.3;q32.3) in multiple myeloma is associated with increased expression and activating mutations of fibroblast growth factor receptor 3. Nature Genet. 16: 260-264, 1997. ; and

[12831] Richelda, R.; Ronchetti, D.; Baldini, L.; Cro, L.; Viggiano, L.; Marzella, R.; Rocchi, M.; Otsuki, T.; Lombardi, L.; Maiolo, A. T.; Neri, A. : A novel chromosomal translocation t(4;14)(p16.

[12832] Further studies establishing the function and utilities of WHSC1 are found in John Hopkins OMIM database record ID 602952, and in cited publications numbered 1060, 1137 and 7987 listed in the bibliography section herein-below, which are also hereby incorporated by reference. Betaine-homocysteine Methyltransferase (BHMT, Ac-

cession NM_001713) is another VGAM200 host target gene. BHMT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHMT BINDING SITE, designated SEQ ID:7443, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12833] Another function of VGAM200 is therefore inhibition of Betaine-homocysteine Methyltransferase (BHMT, Accession NM_001713). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHMT. Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837) is another VGAM200 host target gene. C1orf16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1orf16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1orf16 BINDING SITE, designated SEQ ID:16858, to the nucleotide sequence of VGAM200 RNA, herein designated

VGAM RNA, also designated SEQ ID:2911.

[12834] Another function of VGAM200 is therefore inhibition of Chromosome 1 Open Reading Frame 16 (C1orf16, Accession NM_014837). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1orf16. Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072) is another VGAM200 host target gene. C1QR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C1QR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QR1 BINDING SITE, designated SEQ ID:14340, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12835] Another function of VGAM200 is therefore inhibition of Complement Component 1, Q Subcomponent, Receptor 1 (C1QR1, Accession NM_012072). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QR1. Chromosome 20 Open Reading Frame 28 (C20orf28, Ac-

cession NM_015417) is another VGAM200 host target gene. C20orf28 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C20orf28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf28 BINDING SITE, designated SEQ ID:17720, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12836] Another function of VGAM200 is therefore inhibition of Chromosome 20 Open Reading Frame 28 (C20orf28, Accession NM_015417). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf28. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332) is another VGAM200 host target gene. CDC14B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CDC14B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE, designated SEQ

ID:27175, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12837] Another function of VGAM200 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_033332). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. Calsyntenin 1 (CLSTN1, Accession NM_014944) is another VGAM200 host target gene. CLSTN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLSTN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLSTN1 BINDING SITE, designated SEQ ID:17257, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12838] Another function of VGAM200 is therefore inhibition of Calsyntenin 1 (CLSTN1, Accession NM_014944). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLSTN1. CXYorf1 (Accession XM_088704) is an-

other VGAM200 host target gene. CXYorf1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CXYorf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXYorf1 BINDING SITE, designated SEQ ID:39914, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12839] Another function of VGAM200 is therefore inhibition of CXYorf1 (Accession XM_088704). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXYorf1. DKFZp434G179 (Accession XM_087065) is another VGAM200 host target gene. DKFZp434G179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434G179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434G179 BINDING SITE, designated SEQ ID:39043, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12840] Another function of VGAM200 is therefore inhibition of DKFZp434G179 (Accession XM_087065). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434G179. DKFZp566D133 (Accession XM_050005) is another VGAM200 host target gene. DKFZp566D133 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp566D133, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp566D133 BINDING SITE, designated SEQ ID:35544, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12841] Another function of VGAM200 is therefore inhibition of DKFZp566D133 (Accession XM_050005). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp566D133. DKFZP586F1524 (Accession NM_015584) is another VGAM200 host target gene. DKFZP586F1524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

DKFZP586F1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586F1524 BINDING SITE, designated SEQ ID:17854, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12842] Another function of VGAM200 is therefore inhibition of DKFZP586F1524 (Accession NM_015584). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586F1524. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295) is another VGAM200 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34946, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12843] Another function of VGAM200 is therefore inhibition of

Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ12229 (Accession NM_024876) is another VGAM200 host target gene. FLJ12229 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ12229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12229 BINDING SITE, designated SEQ ID:24310, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12844] Another function of VGAM200 is therefore inhibition of FLJ12229 (Accession NM_024876). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12229. FLJ12529 (Accession NM_024811) is another VGAM200 host target gene. FLJ12529 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12529, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12529 BINDING SITE, designated SEQ ID:24192, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12845] Another function of VGAM200 is therefore inhibition of FLJ12529 (Accession NM_024811). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12529. FLJ12688 (Accession XM_055071) is another VGAM200 host target gene. FLJ12688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12688 BINDING SITE, designated SEQ ID:36222, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12846] Another function of VGAM200 is therefore inhibition of FLJ12688 (Accession XM_055071). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12688.

FLJ14708 (Accession NM_032827) is another VGAM200 host target gene. FLJ14708 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14708, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14708 BINDING SITE, designated SEQ ID:26601, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12847] Another function of VGAM200 is therefore inhibition of FLJ14708 (Accession NM_032827). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14708. FLJ14855 (Accession NM_033210) is another VGAM200 host target gene. FLJ14855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14855 BINDING SITE, designated SEQ ID:27059, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2911.

[12848] Another function of VGAM200 is therefore inhibition of FLJ14855 (Accession NM_033210). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14855. FLJ20069 (Accession NM_017651) is another VGAM200 host target gene. FLJ20069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20069 BINDING SITE, designated SEQ ID:19158, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12849] Another function of VGAM200 is therefore inhibition of FLJ20069 (Accession NM_017651). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20069. FLJ20232 (Accession NM_019008) is another VGAM200 host target gene. FLJ20232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20232, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20232 BINDING SITE, designated SEQ ID:21087, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12850] Another function of VGAM200 is therefore inhibition of FLJ20232 (Accession NM_019008). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20232. FLJ20294 (Accession NM_017749) is another VGAM200 host target gene. FLJ20294 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20294 BINDING SITE, designated SEQ ID:19348, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12851] Another function of VGAM200 is therefore inhibition of FLJ20294 (Accession NM_017749). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ20294. FLJ20507 (Accession NM_017849) is another VGAM200 host target gene. FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20507, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20507 BINDING SITE1 and FLJ20507 BINDING SITE2, designated SEQ ID:19514 and SEQ ID:30222 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12852] Another function of VGAM200 is therefore inhibition of FLJ20507 (Accession NM_017849). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20507. FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513) is another VGAM200 host target gene. FYCO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FYCO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FYCO1 BINDING SITE, designated SEQ ID:23707, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12853] Another function of VGAM200 is therefore inhibition of FYVE and Coiled-coil Domain Containing 1 (FYCO1, Accession NM_024513). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FYCO1. Growth Differentiation Factor 10 (GDF10, Accession NM_004962) is another VGAM200 host target gene. GDF10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GDF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GDF10 BINDING SITE, designated SEQ ID:11410, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12854] Another function of VGAM200 is therefore inhibition of Growth Differentiation Factor 10 (GDF10, Accession NM_004962). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with GDF10. GMPPB (Accession XM_171044) is another VGAM200 host target gene. GMPPB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GMPPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMPPB BINDING SITE, designated SEQ ID:45820, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12855] Another function of VGAM200 is therefore inhibition of GMPPB (Accession XM_171044). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMPPB. HCCA2 (Accession XM_039894) is another VGAM200 host target gene. HCCA2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HCCA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HCCA2 BINDING SITE, designated SEQ ID:33204, to the nucleotide sequence of VGAM200

RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12856] Another function of VGAM200 is therefore inhibition of HCCA2 (Accession XM_039894). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HCCA2. Interleukin 14 (IL14, Accession XM_170924) is another VGAM200 host target gene. IL14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL14 BINDING SITE, designated SEQ ID:45706, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12857] Another function of VGAM200 is therefore inhibition of Interleukin 14 (IL14, Accession XM_170924). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL14. ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM_047951) is another VGAM200 host target gene. ISL2 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by ISL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ISL2 BINDING SITE, designated SEQ ID:35082, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12858] Another function of VGAM200 is therefore inhibition of ISL2 Transcription Factor, LIM/homeodomain, (islet-2) (ISL2, Accession XM_047951). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ISL2. Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186) is another VGAM200 host target gene. KCNB2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNB2 BINDING SITE, designated SEQ ID:45965, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2911.

[12859] Another function of VGAM200 is therefore inhibition of Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNB2. KIAA0040 (Accession NM_014656) is another VGAM200 host target gene. KIAA0040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0040 BINDING SITE, designated SEQ ID:16095, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12860] Another function of VGAM200 is therefore inhibition of KIAA0040 (Accession NM_014656). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0040. KIAA0237 (Accession NM_014747) is another VGAM200 host target gene. KIAA0237 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0237, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0237 BINDING SITE, designated SEQ ID:16457, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12861] Another function of VGAM200 is therefore inhibition of KIAA0237 (Accession NM_014747). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0237. KIAA0415 (Accession XM_166527) is another VGAM200 host target gene. KIAA0415 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0415, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0415 BINDING SITE, designated SEQ ID:44478, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12862] Another function of VGAM200 is therefore inhibition of KIAA0415 (Accession XM_166527). Accordingly, utilities

of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0415. KIAA0469 (Accession NM_014851) is another VGAM200 host target gene. KIAA0469 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0469 BINDING SITE, designated SEQ ID:16898, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12863] Another function of VGAM200 is therefore inhibition of KIAA0469 (Accession NM_014851). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0469. KIAA0495 (Accession XM_031397) is another VGAM200 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0495 BINDING SITE, designated SEQ ID:31359, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12864] Another function of VGAM200 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0495. KIAA0574 (Accession XM_045076) is another VGAM200 host target gene. KIAA0574 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0574, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0574 BINDING SITE, designated SEQ ID:34349, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12865] Another function of VGAM200 is therefore inhibition of KIAA0574 (Accession XM_045076). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0574. KIAA0763 (Accession NM_014869) is another VGAM200 host target gene. KIAA0763 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0763 BINDING SITE, designated SEQ ID:16972, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12866] Another function of VGAM200 is therefore inhibition of KIAA0763 (Accession NM_014869). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0763. KIAA0773 (Accession NM_014690) is another VGAM200 host target gene. KIAA0773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0773 BINDING SITE, designated SEQ ID:16195, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12867] Another function of VGAM200 is therefore inhibition of

KIAA0773 (Accession NM_014690). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0773. KIAA0930 (Accession XM_047214) is another VGAM200 host target gene. KIAA0930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0930 BINDING SITE, designated SEQ ID:34914, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12868] Another function of VGAM200 is therefore inhibition of KIAA0930 (Accession XM_047214). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0930. KIAA0939 (Accession XM_030524) is another VGAM200 host target gene. KIAA0939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0939 BINDING SITE, designated SEQ ID:31059, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12869] Another function of VGAM200 is therefore inhibition of KIAA0939 (Accession XM_030524). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0939. KIAA1014 (Accession XM_037205) is another VGAM200 host target gene. KIAA1014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1014 BINDING SITE, designated SEQ ID:32571, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12870] Another function of VGAM200 is therefore inhibition of KIAA1014 (Accession XM_037205). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1014. KIAA1297 (Accession XM_051005) is another

VGAM200 host target gene. KIAA1297 BINDING SITE1 and KIAA1297 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1297, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE1 and KIAA1297 BINDING SITE2, designated SEQ ID:35722 and SEQ ID:35723 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12871] Another function of VGAM200 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1297. KIAA1649 (Accession NM_032311) is another VGAM200 host target gene. KIAA1649 BINDING SITE1 and KIAA1649 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1649, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1649 BINDING SITE1 and KIAA1649

BINDING SITE2, designated SEQ ID:26107 and SEQ ID:33256 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12872] Another function of VGAM200 is therefore inhibition of KIAA1649 (Accession NM_032311). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. KIAA1870 (Accession NM_032888) is another VGAM200 host target gene. KIAA1870 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1870 BINDING SITE, designated SEQ ID:26708, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12873] Another function of VGAM200 is therefore inhibition of KIAA1870 (Accession NM_032888). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1870. KIAA1884 (Accession XM_055539) is another

VGAM200 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36294, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12874] Another function of VGAM200 is therefore inhibition of KIAA1884 (Accession XM_055539). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. KIAA1944 (Accession XM_062545) is another VGAM200 host target gene. KIAA1944 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1944, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1944 BINDING SITE, designated SEQ ID:37227, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12875] Another function of VGAM200 is therefore inhibition of KIAA1944 (Accession XM_062545). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1944. Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379) is another VGAM200 host target gene. MAN1C1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAN1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1C1 BINDING SITE, designated SEQ ID:21646, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12876] Another function of VGAM200 is therefore inhibition of Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1C1. MGC19556 (Accession NM_033551) is another VGAM200 host target gene. MGC19556 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of

mRNA encoded by MGC19556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC19556 BINDING SITE, designated SEQ ID:27318, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12877] Another function of VGAM200 is therefore inhibition of MGC19556 (Accession NM_033551). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC19556. MGC20460 (Accession NM_053043) is another VGAM200 host target gene. MGC20460 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20460, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20460 BINDING SITE, designated SEQ ID:27587, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12878] Another function of VGAM200 is therefore inhibition of MGC20460 (Accession NM_053043). Accordingly, utilities

of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20460. MICAL (Accession NM_022765) is another VGAM200 host target gene. MICAL BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MICAL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MICAL BINDING SITE, designated SEQ ID:23011, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12879] Another function of VGAM200 is therefore inhibition of MICAL (Accession NM_022765). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MICAL. My015 (Accession XM_039512) is another VGAM200 host target gene. My015 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by My015, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of My015 BINDING SITE, designated SEQ

ID:33108, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12880] Another function of VGAM200 is therefore inhibition of My015 (Accession XM_039512). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with My015. Myelin Transcription Factor 1 (MYT1, Accession NM_004535) is another VGAM200 host target gene. MYT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYT1 BINDING SITE, designated SEQ ID:10875, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12881] Another function of VGAM200 is therefore inhibition of Myelin Transcription Factor 1 (MYT1, Accession NM_004535). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYT1. Phosphate Cytidylyltransferase 2, Ethanolamine (PCYT2, Accession

NM_002861) is another VGAM200 host target gene.

PCYT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCYT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCYT2 BINDING SITE, designated SEQ ID:8762, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12882] Another function of VGAM200 is therefore inhibition of Phosphate Cytidylyltransferase 2, Ethanolamine (PCYT2, Accession NM_002861). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCYT2. Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM_138687) is another VGAM200 host target gene. PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIP5K2B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2, des-

ignated SEQ ID:28929 and SEQ ID:9607 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12883] Another function of VGAM200 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM_138687). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K2B. Phosphatidylserine Decarboxylase (PISD, Accession NM_014338) is another VGAM200 host target gene. PISD BINDING SITE1 and PISD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PISD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PISD BINDING SITE1 and PISD BINDING SITE2, designated SEQ ID:15658 and SEQ ID:18234 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12884] Another function of VGAM200 is therefore inhibition of Phosphatidylserine Decarboxylase (PISD, Accession NM_014338). Accordingly, utilities of VGAM200 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with PISD. PRO1163 (Accession NM_018576) is another VGAM200 host target gene.

PRO1163 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1163, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1163 BINDING SITE, designated SEQ ID:20655, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12885] Another function of VGAM200 is therefore inhibition of PRO1163 (Accession NM_018576). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1163. Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564) is another VGAM200 host target gene. SLC39A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC39A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of SLC39A3 BINDING SITE, designated SEQ ID:29362, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12886] Another function of VGAM200 is therefore inhibition of Solute Carrier Family 39 (zinc transporter), Member 3 (SLC39A3, Accession NM_144564). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC39A3. TED (Accession NM_015686) is another VGAM200 host target gene. TED BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TED, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TED BINDING SITE, designated SEQ ID:17918, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12887] Another function of VGAM200 is therefore inhibition of TED (Accession NM_015686). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TED.

Testis Specific, 14 (TSGA14, Accession NM_018718) is another VGAM200 host target gene. TSGA14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSGA14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSGA14 BINDING SITE, designated SEQ ID:20796, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12888] Another function of VGAM200 is therefore inhibition of Testis Specific, 14 (TSGA14, Accession NM_018718). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSGA14. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM200 host target gene. ZDHHC2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18489, to the nucleotide

sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12889] Another function of VGAM200 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC115073 (Accession XM_055193) is another VGAM200 host target gene. LOC115073 BINDING SITE1 and LOC115073 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC115073, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115073 BINDING SITE1 and LOC115073 BINDING SITE2, designated SEQ ID:36243 and SEQ ID:36244 respectively, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12890] Another function of VGAM200 is therefore inhibition of LOC115073 (Accession XM_055193). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC115073. LOC129138 (Accession NM_138797) is another VGAM200 host target gene. LOC129138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129138 BINDING SITE, designated SEQ ID:29020, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12891] Another function of VGAM200 is therefore inhibition of LOC129138 (Accession NM_138797). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129138. LOC132235 (Accession XM_072302) is another VGAM200 host target gene. LOC132235 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC132235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132235 BINDING SITE, designated SEQ ID:37484, to the nucleotide sequence of VGAM200 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2911.

[12892] Another function of VGAM200 is therefore inhibition of LOC132235 (Accession XM_072302). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132235. LOC143310 (Accession XM_084485) is another VGAM200 host target gene. LOC143310 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143310 BINDING SITE, designated SEQ ID:37608, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12893] Another function of VGAM200 is therefore inhibition of LOC143310 (Accession XM_084485). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143310. LOC144317 (Accession XM_084813) is another VGAM200 host target gene. LOC144317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144317, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144317 BINDING SITE, designated SEQ ID:37719, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12894] Another function of VGAM200 is therefore inhibition of LOC144317 (Accession XM_084813). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144317. LOC144699 (Accession XM_084940) is another VGAM200 host target gene. LOC144699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144699 BINDING SITE, designated SEQ ID:37770, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12895] Another function of VGAM200 is therefore inhibition of LOC144699 (Accession XM_084940). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC144699. LOC145717 (Accession XM_039771) is another VGAM200 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33191, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12896] Another function of VGAM200 is therefore inhibition of LOC145717 (Accession XM_039771). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC146520 (Accession XM_085492) is another VGAM200 host target gene. LOC146520 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146520, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146520 BINDING SITE, designated SEQ ID:38189, to

the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12897] Another function of VGAM200 is therefore inhibition of LOC146520 (Accession XM_085492). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146520. LOC147664 (Accession XM_085826) is another VGAM200 host target gene. LOC147664 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147664, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147664 BINDING SITE, designated SEQ ID:38353, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12898] Another function of VGAM200 is therefore inhibition of LOC147664 (Accession XM_085826). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147664. LOC148029 (Accession XM_086014) is another VGAM200 host target gene. LOC148029 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC148029, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148029 BINDING SITE, designated SEQ ID:38448, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12899] Another function of VGAM200 is therefore inhibition of LOC148029 (Accession XM_086014). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148029. LOC149950 (Accession XM_086732) is another VGAM200 host target gene. LOC149950 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149950 BINDING SITE, designated SEQ ID:38841, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12900] Another function of VGAM200 is therefore inhibition of LOC149950 (Accession XM_086732). Accordingly, utilities

of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149950. LOC150245 (Accession XM_097843) is another VGAM200 host target gene. LOC150245 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC150245, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150245 BINDING SITE, designated SEQ ID:41165, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12901] Another function of VGAM200 is therefore inhibition of LOC150245 (Accession XM_097843). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150245. LOC152992 (Accession XM_087575) is another VGAM200 host target gene. LOC152992 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC152992, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC152992 BINDING SITE, designated SEQ ID:39351, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12902] Another function of VGAM200 is therefore inhibition of LOC152992 (Accession XM_087575). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152992. LOC154092 (Accession XM_098466) is another VGAM200 host target gene. LOC154092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154092 BINDING SITE, designated SEQ ID:41682, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12903] Another function of VGAM200 is therefore inhibition of LOC154092 (Accession XM_098466). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154092. LOC158428 (Accession XM_047249) is another VGAM200 host target gene. LOC158428 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158428, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158428 BINDING SITE, designated SEQ ID:34923, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12904] Another function of VGAM200 is therefore inhibition of LOC158428 (Accession XM_047249). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158428. LOC158434 (Accession XM_098939) is another VGAM200 host target gene. LOC158434 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158434 BINDING SITE, designated SEQ ID:41987, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12905] Another function of VGAM200 is therefore inhibition of

LOC158434 (Accession XM_098939). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158434. LOC158515 (Accession XM_092979) is another VGAM200 host target gene. LOC158515 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158515 BINDING SITE, designated SEQ ID:40162, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12906] Another function of VGAM200 is therefore inhibition of LOC158515 (Accession XM_092979). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158515. LOC161635 (Accession XM_172921) is another VGAM200 host target gene. LOC161635 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC161635, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC161635 BINDING SITE, designated SEQ ID:46186, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12907] Another function of VGAM200 is therefore inhibition of LOC161635 (Accession XM_172921). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC161635. LOC195977 (Accession XM_113625) is another VGAM200 host target gene. LOC195977 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC195977, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC195977 BINDING SITE, designated SEQ ID:42301, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12908] Another function of VGAM200 is therefore inhibition of LOC195977 (Accession XM_113625). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC195977. LOC199786 (Accession XM_114021) is an-

other VGAM200 host target gene. LOC199786 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199786, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199786 BINDING SITE, designated SEQ ID:42622, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12909] Another function of VGAM200 is therefore inhibition of LOC199786 (Accession XM_114021). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199786. LOC200093 (Accession XM_032184) is another VGAM200 host target gene. LOC200093 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200093, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200093 BINDING SITE, designated SEQ ID:31606, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12910] Another function of VGAM200 is therefore inhibition of LOC200093 (Accession XM_032184). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200093. LOC200138 (Accession XM_117194) is another VGAM200 host target gene. LOC200138 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200138 BINDING SITE, designated SEQ ID:43280, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12911] Another function of VGAM200 is therefore inhibition of LOC200138 (Accession XM_117194). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200138. LOC200918 (Accession XM_114316) is another VGAM200 host target gene. LOC200918 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200918, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200918 BINDING SITE, designated SEQ ID:42870, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12912] Another function of VGAM200 is therefore inhibition of LOC200918 (Accession XM_114316). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200918. LOC205418 (Accession XM_119792) is another VGAM200 host target gene. LOC205418 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205418 BINDING SITE, designated SEQ ID:43598, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12913] Another function of VGAM200 is therefore inhibition of LOC205418 (Accession XM_119792). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC205418. LOC220980 (Accession XM_167629) is another VGAM200 host target gene. LOC220980 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220980 BINDING SITE, designated SEQ ID:44741, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12914] Another function of VGAM200 is therefore inhibition of LOC220980 (Accession XM_167629). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220980. LOC221751 (Accession XM_166370) is another VGAM200 host target gene. LOC221751 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221751, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221751 BINDING SITE, designated SEQ ID:44189, to the nucleotide sequence of VGAM200 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2911.

[12915] Another function of VGAM200 is therefore inhibition of LOC221751 (Accession XM_166370). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221751. LOC245727 (Accession XM_165913) is another VGAM200 host target gene. LOC245727 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC245727, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245727 BINDING SITE, designated SEQ ID:43796, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12916] Another function of VGAM200 is therefore inhibition of LOC245727 (Accession XM_165913). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245727. LOC253001 (Accession XM_171711) is another VGAM200 host target gene. LOC253001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253001, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46059, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12917] Another function of VGAM200 is therefore inhibition of LOC253001 (Accession XM_171711). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253001. LOC253070 (Accession XM_173088) is another VGAM200 host target gene. LOC253070 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253070 BINDING SITE, designated SEQ ID:46353, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12918] Another function of VGAM200 is therefore inhibition of LOC253070 (Accession XM_173088). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC253070. LOC253805 (Accession XM_172854) is another VGAM200 host target gene. LOC253805 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253805, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253805 BINDING SITE, designated SEQ ID:46138, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12919] Another function of VGAM200 is therefore inhibition of LOC253805 (Accession XM_172854). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253805. LOC253959 (Accession XM_170749) is another VGAM200 host target gene. LOC253959 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253959, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253959 BINDING SITE, designated SEQ ID:45510, to

the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12920] Another function of VGAM200 is therefore inhibition of LOC253959 (Accession XM_170749). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253959. LOC254387 (Accession XM_170731) is another VGAM200 host target gene. LOC254387 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254387, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254387 BINDING SITE, designated SEQ ID:45489, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12921] Another function of VGAM200 is therefore inhibition of LOC254387 (Accession XM_170731). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254387. LOC254532 (Accession XM_172961) is another VGAM200 host target gene. LOC254532 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC254532, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254532 BINDING SITE, designated SEQ ID:46208, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12922] Another function of VGAM200 is therefore inhibition of LOC254532 (Accession XM_172961). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254532. LOC255650 (Accession XM_172981) is another VGAM200 host target gene. LOC255650 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255650, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255650 BINDING SITE, designated SEQ ID:46248, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12923] Another function of VGAM200 is therefore inhibition of LOC255650 (Accession XM_172981). Accordingly, utilities

of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255650. LOC256158 (Accession XM_175125) is another VGAM200 host target gene. LOC256158 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC256158, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256158 BINDING SITE, designated SEQ ID:46633, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12924] Another function of VGAM200 is therefore inhibition of LOC256158 (Accession XM_175125). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256158. LOC256248 (Accession XM_172550) is another VGAM200 host target gene. LOC256248 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC256248, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC256248 BINDING SITE, designated SEQ ID:46075, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12925] Another function of VGAM200 is therefore inhibition of LOC256248 (Accession XM_172550). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256248. LOC256790 (Accession XM_170679) is another VGAM200 host target gene. LOC256790 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256790, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256790 BINDING SITE, designated SEQ ID:45461, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12926] Another function of VGAM200 is therefore inhibition of LOC256790 (Accession XM_170679). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256790. LOC89958 (Accession XM_027627) is another VGAM200 host target gene. LOC89958 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC89958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89958 BINDING SITE, designated SEQ ID:30544, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12927] Another function of VGAM200 is therefore inhibition of LOC89958 (Accession XM_027627). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89958. LOC90362 (Accession XM_031163) is another VGAM200 host target gene. LOC90362 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90362 BINDING SITE, designated SEQ ID:31296, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12928] Another function of VGAM200 is therefore inhibition of

LOC90362 (Accession XM_031163). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90362. LOC90678 (Accession NM_138361) is another VGAM200 host target gene. LOC90678 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90678, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90678 BINDING SITE, designated SEQ ID:28748, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12929] Another function of VGAM200 is therefore inhibition of LOC90678 (Accession NM_138361). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90678. LOC90841 (Accession XM_034427) is another VGAM200 host target gene. LOC90841 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC90841 BINDING SITE, designated SEQ ID:32114, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12930] Another function of VGAM200 is therefore inhibition of LOC90841 (Accession XM_034427). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90841. LOC90925 (Accession XM_034917) is another VGAM200 host target gene. LOC90925 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90925, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90925 BINDING SITE, designated SEQ ID:32187, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12931] Another function of VGAM200 is therefore inhibition of LOC90925 (Accession XM_034917). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90925. LOC91040 (Accession XM_035641) is another

VGAM200 host target gene. LOC91040 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91040 BINDING SITE, designated SEQ ID:32323, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12932] Another function of VGAM200 is therefore inhibition of LOC91040 (Accession XM_035641). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91040. LOC91409 (Accession XM_038298) is another VGAM200 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32807, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12933] Another function of VGAM200 is therefore inhibition of LOC91409 (Accession XM_038298). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. LOC91663 (Accession NM_138373) is another VGAM200 host target gene. LOC91663 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91663 BINDING SITE, designated SEQ ID:28754, to the nucleotide sequence of VGAM200 RNA, herein designated VGAM RNA, also designated SEQ ID:2911.

[12934] Another function of VGAM200 is therefore inhibition of LOC91663 (Accession NM_138373). Accordingly, utilities of VGAM200 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91663. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 201 (VGAM201) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[12935] VGAM201 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM201 was detected is described hereinabove with reference to Figs. 1–8.

[12936] VGAM201 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12937] VGAM201 gene encodes a VGAM201 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM201 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM201 precursor RNA is designated SEQ ID:187, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:187 is located at position 124735 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12938] VGAM201 precursor RNA folds onto itself, forming

VGAM201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12939] An enzyme complex designated DICER COMPLEX, `dices` the VGAM201 folded precursor RNA into VGAM201 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM201 RNA is designated SEQ ID:2912, and is provided hereinbelow with reference to the sequence listing part.

[12940] VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM201 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12941] VGAM201 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM201 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM201 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12942] The complementary binding of VGAM201 RNA, herein designated VGAM RNA, to host target binding sites on VGAM201 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM201 host target RNA into VGAM201 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12943] It is appreciated that VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM201 host target genes. The mRNA of each one of this plurality of VGAM201 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM201 RNA, herein designated VGAM RNA, and which when bound by VGAM201 RNA causes inhibition of translation of respective one or more VGAM201 host target proteins.

[12944] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM201 gene, herein designated VGAM GENE, on one or more VGAM201 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12945] It is yet further appreciated that a function of VGAM201 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM201 correlate with, and may be deduced from, the identity of the host

target genes which VGAM201 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [12946] Nucleotide sequences of the VGAM201 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM201 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM201 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM201 are further described hereinbelow with reference to Table 1.
- [12947] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM201 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM201 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [12948] As mentioned hereinabove with reference to Fig. 1, a function of VGAM201 gene, herein designated VGAM is inhibition of expression of VGAM201 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM201 correlate with, and may be deduced from, the identity of the target genes which VGAM201

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12949] FCRH1 (Accession NM_052938) is a VGAM201 host target gene. FCRH1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FCRH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCRH1 BINDING SITE, designated SEQ ID:27496, to the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, also designated SEQ ID:2912.

[12950] A function of VGAM201 is therefore inhibition of FCRH1 (Accession NM_052938). Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCRH1. Transient Receptor Potential Cation Channel, Subfamily M, Member 8 (TRPM8, Accession NM_024080) is another VGAM201 host target gene. TRPM8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TRPM8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of TRPM8 BINDING SITE, designated SEQ ID:23512, to the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, also designated SEQ ID:2912.

[12951] Another function of VGAM201 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 8 (TRPM8, Accession NM_024080), a gene which is thought to form a receptor-activated calcium permeant cation channel. Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM8. The function of TRPM8 has been established by previous studies. Using expression cloning of a rat trigeminal nerve cDNA library in a human embryonic kidney cell line and screening for changes in intracellular calcium on exposure to room-temperature menthol, McKemy et al. (2002) identified a cDNA encoding Cmr1 (cold-menthol receptor-1). The deduced 1,104-amino acid protein, 92% identical to human TRPM8, is also responsive to icilin, cold (with a range from 8 to 28 degrees C), and eucalyptol (the main constituent of oil of Eucalyptus) with low or no responses to menthone, camphor, cyclohexanol, or capsaicin, the agonist for VR1, which is related to the TRP family. Northern blot

analysis detected transcripts of 6.0 and 4.5 kb in rat dorsal root ganglia and trigeminal neurons. In situ hybridization analysis demonstrated expression in small-diameter, but not larger-diameter, sensory neurons, similar in size to VR1-expressing cells. Cells expressing both Cmr1 and Vr1 endow cells to respond to distinct temperature thresholds, cool and hot (more than 43 degrees C), respectively. McKemy et al. (2002) suggested this coexpression may explain the paradox that noxious cold is sometimes perceived as burning pain. The authors also proposed that in other contexts, such as prostate and tumors, an endogenous menthol-like ligand may modulate the TRPM8 channel. Peier et al. (2002) showed that mouse Trpm8 is specifically expressed in a subset of pain- and temperature-sensing neurons. Cells overexpressing the Trpm8 channel could be activated by cold temperatures and by a cooling agent, menthol. The authors concluded that the identification of a cold-sensing TRP channel in a distinct subpopulation of sensory neurons implicated an expanded role for this family of ion channels in somatic sensory detection.

[12952] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [12953] McKemy, D. D.; Neuhausser, W. M.; Julius, D. : Identification of a cold receptor reveals a general role for TRP channels in thermosensation. *Nature* 416: 52–58, 2002. ; and
- [12954] Peier, A. M.; Moqrich, A.; Hergarden, A. C.; Reeve, A. J.; Andersson, D. A.; Story, G. M.; Earley, T. J.; Dragoni, I.; McIntyre, P.; Bevan, S.; Patapoutian, A. : A TRP channel that sense.
- [12955] Further studies establishing the function and utilities of TRPM8 are found in John Hopkins OMIM database record ID 606678, and in cited publications numbered 5545–554 and 4909 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC154222 (Accession XM_098497) is another VGAM201 host target gene. LOC154222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154222 BINDING SITE, designated SEQ ID:41688, to the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, also designated SEQ ID:2912.

[12956] Another function of VGAM201 is therefore inhibition of LOC154222 (Accession XM_098497). Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154222. LOC221814 (Accession XM_168226) is another VGAM201 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45089, to the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, also designated SEQ ID:2912.

[12957] Another function of VGAM201 is therefore inhibition of LOC221814 (Accession XM_168226). Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. LOC91397 (Accession XM_038219) is another VGAM201 host target gene. LOC91397 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91397, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91397 BINDING SITE, designated SEQ ID:32778, to the nucleotide sequence of VGAM201 RNA, herein designated VGAM RNA, also designated SEQ ID:2912.

[12958] Another function of VGAM201 is therefore inhibition of LOC91397 (Accession XM_038219). Accordingly, utilities of VGAM201 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91397. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 202 (VGAM202) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12959] VGAM202 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM202 was detected is described hereinabove with reference to Figs. 1–8.

[12960] VGAM202 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM202 host

target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12961] VGAM202 gene encodes a VGAM202 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM202 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM202 precursor RNA is designated SEQ ID:188, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:188 is located at position 276485 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12962] VGAM202 precursor RNA folds onto itself, forming VGAM202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12963] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM202 folded precursor RNA into VGAM202 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM202 RNA is designated SEQ ID:2913, and is provided hereinbelow with reference to the sequence listing part.

[12964] VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM202 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12965] VGAM202 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM202 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM202 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12966] The complementary binding of VGAM202 RNA, herein designated VGAM RNA, to host target binding sites on VGAM202 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM202 host target RNA into VGAM202 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12967] It is appreciated that VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM202 host target genes. The mRNA of each one of this plurality of VGAM202 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM202 RNA, herein designated VGAM RNA, and which when bound by VGAM202 RNA causes inhibition of translation of respective one or more VGAM202 host target proteins.

[12968] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM202 gene, herein designated VGAM GENE, on one or more VGAM202 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12969] It is yet further appreciated that a function of VGAM202 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM202 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM202 correlate with, and may be deduced from, the identity of the host target genes which VGAM202 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12970] Nucleotide sequences of the VGAM202 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM202 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM202 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM202 are further

described hereinbelow with reference to Table 1.

[12971] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM202 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM202 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12972] As mentioned hereinabove with reference to Fig. 1, a function of VGAM202 gene, herein designated VGAM is inhibition of expression of VGAM202 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM202 correlate with, and may be deduced from, the identity of the target genes which VGAM202 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12973] Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM_085082) is a VGAM202 host target gene. ARHGAP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGAP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of ARHGAP5 BINDING SITE, designated SEQ ID:37815, to the nucleotide sequence of VGAM202 RNA, herein designated VGAM RNA, also designated SEQ ID:2913.

[12974] A function of VGAM202 is therefore inhibition of Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM_085082). Accordingly, utilities of VGAM202 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP5. PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM_028335) is another VGAM202 host target gene. PRPF8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRPF8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRPF8 BINDING SITE, designated SEQ ID:30675, to the nucleotide sequence of VGAM202 RNA, herein designated VGAM RNA, also designated SEQ ID:2913.

[12975] Another function of VGAM202 is therefore inhibition of PRP8 Pre-mRNA Processing Factor 8 Homolog (yeast) (PRPF8, Accession XM_028335). Accordingly, utilities of VGAM202 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with PRPF8.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 203 (VGAM203) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[12976] VGAM203 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM203 was detected is described hereinabove with reference to Figs. 1–8.

[12977] VGAM203 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[12978] VGAM203 gene encodes a VGAM203 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM203 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM203 precursor RNA is designated SEQ ID:189, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:189 is located at position 64186 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[12979] VGAM203 precursor RNA folds onto itself, forming VGAM203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[12980] An enzyme complex designated DICER COMPLEX, `dices` the VGAM203 folded precursor RNA into VGAM203 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 51%) nucleotide sequence of VGAM203 RNA is designated SEQ ID:2914, and is provided hereinbelow with reference to the sequence

listing part.

[12981] VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM203 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[12982] VGAM203 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM203 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM203 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[12983] The complementary binding of VGAM203 RNA, herein designated VGAM RNA, to host target binding sites on VGAM203 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM203 host target RNA into VGAM203 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[12984] It is appreciated that VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM203 host target genes. The mRNA of each one of this plurality of VGAM203 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM203 RNA, herein designated VGAM

RNA, and which when bound by VGAM203 RNA causes inhibition of translation of respective one or more VGAM203 host target proteins.

[12985] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM203 gene, herein designated VGAM GENE, on one or more VGAM203 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[12986] It is yet further appreciated that a function of VGAM203 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM203 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM203 correlate with, and may be deduced from, the identity of the host target genes which VGAM203 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[12987] Nucleotide sequences of the VGAM203 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM203 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM203 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM203 are further described hereinbelow with reference to Table 1.

[12988] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM203 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM203 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[12989] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM203 gene, herein designated VGAM is inhibition of expression of VGAM203 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM203 correlate with, and may be deduced from, the identity of the target genes which VGAM203 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[12990] Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM_006030) is a VGAM203 host target gene. CACNA2D2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNA2D2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA2D2 BINDING SITE, designated SEQ ID:12646, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[12991] A function of VGAM203 is therefore inhibition of Calcium Channel, Voltage-dependent, Alpha 2/delta Subunit 2 (CACNA2D2, Accession NM_006030), a gene which is a calcium channel protein which plays an important role in excitation-contraction coupling. Accordingly, utilities of

VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA2D2. The function of CACNA2D2 has been established by previous studies. By physical cloning methodologies and bioinformatic computational analyses, Lerman and Minna (2000) identified a number of genes, including CACNA2D2, in a region of chromosome 3p21.3 that is associated with a putative lung cancer tumor suppressor gene. They did not detect CACNA2D2 mutations in any lung cancer cell lines tested. Animal model experiments lend further support to the function of CACNA2D2. Brodbeck et al. (2002) showed that mice with the 'duffy' (du) mutation, a model for absence epilepsy (see OMIM Ref. No. 600131), had a mutation in Cacna2d2 gene. The mutation resulted in the introduction of a premature stop codon and the expression of a truncated protein encoded by the first 3 exons of Cacna2d2, followed by 8 novel amino acids. The shortened mRNA and protein were expressed in mutant mouse cerebellum and Purkinje cells. Brodbeck et al. (2002) detected high expression of the normal protein in cerebellar Purkinje cells, but found that duffy mice had abnormalities in their Purkinje cell dendritic trees. Functional analysis indicated that the mutant

Cacna2d2 protein failed to increase or even decreased the peak current density of the voltage-gated Ca(V)2.1 (CACNA1A; 601011)/beta-4 (CACNB4; 601949) channel combination, suggesting that it may contribute to the ducky phenotype.

[12992] It is appreciated that the abovementioned animal model for CACNA2D2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[12993] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12994] Brodbeck, J.; Davies, A.; Courtney, J.-M.; Meir, A.; Balaguero, N.; Canti, C.; Moss, F. J.; Page, K. M.; Pratt, W. S.; Hunt, S. P.; Barclay, J.; Rees, M.; Dolphin, A. C. : The ducky mutation in Cacna2d2 results in altered Purkinje cell morphology and is associated with the expression of a truncated alpha-2/delta-2 protein with abnormal function. J. Biol. Chem. 277: 7684-7693, 2002. ; and

[12995] Lerman, M. I.; Minna, J. D. : The 630-kb lung cancer homozygous deletion region on human chromosome 3p21.3: identification and evaluation of the resident candidate tumor suppressor gene.

[12996] Further studies establishing the function and utilities of CACNA2D2 are found in John Hopkins OMIM database record ID 607082, and in cited publications numbered 5491–5492, 10 and 6735 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ferredoxin 1 (FDX1, Accession XM_016467) is another VGAM203 host target gene. FDX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FDX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FDX1 BINDING SITE, designated SEQ ID:30259, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[12997] Another function of VGAM203 is therefore inhibition of Ferredoxin 1 (FDX1, Accession XM_016467), a gene which tcytochromes P450 involved in steroid, vitamin D, and bile acid metabolism. Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FDX1. The function of FDX1 has been established by previous studies. Ferredoxin is a small, acidic, iron–sulfur protein that functions

as an electron transport intermediate for mitochondrial cytochromes P450 involved in steroid, vitamin D, and bile acid metabolism. Electrons are transferred from NADPH through a flavin-containing protein (ferredoxin oxidoreductase) and ferredoxin to the terminal cytochrome P450 for oxidation/reduction reactions. Mitochondrial P450s and their ferredoxin are found mainly in the steroidogenic tissues, including adrenal, ovary, testis, and placenta (Jefcoate et al., 1986). Small amounts of them are also found in the liver and kidney for bile acid and vitamin D synthesis. Because of its relative abundance, the adrenal ferredoxin, designated adrenodoxin, has been characterized in the most detail. It is synthesized as a precursor in which 60 amino acids of the signal peptide are later cleaved upon transport into the mitochondrial inner matrix to form a mature protein of 124 amino acids (Okamura et al., 1985). In almost all human tissues, Morel et al. (1987, 1988) found ADX mRNA in 3 sizes: 1.1, 1.4, and 1.65 kb. Cloning and sequencing of 3 ADX cDNAs showed that the mRNAs of various sizes resulted from alternate polyadenylation sites yielding 3-prime untranslated regions of 229, 530, and 790 bp, respectively. The 540-bp coding region and the 5-prime untranslated re-

gion were identical in all cases. By means of Southern blot analysis of DNA from somatic cell hybrids using stringent conditions of hybridization, 2 chromosomal sites were identified for the ADX gene: chromosomes 11 and 20. One sequence was suspected to represent a processed, intronless pseudogene. Because of the restriction pattern, Morel et al. (1987) suggested that the sequence on chromosome 20 is a pseudogene. Chang et al. (1988) found that the ADX gene spans more than 20 kb and contains 4 exons and 3 introns. The first exon encodes the 60-amino acid signal peptide, which directs transport of the protein into the inner mitochondrial matrix. The mature peptide of 124 amino acids is encoded by the other 3 exons. The third exon encodes the portion of the protein containing the iron-sulfur center and a domain that binds other components of the electron transport chain. By analysis of somatic cell hybrids, Morel et al. (1988) and Chang et al. (1990) assigned the ADX gene to 11q13-qter. Chang et al. (1990) identified pseudogenes on both chromosome 20 and chromosome 21. The pseudogenes lacked introns and contained numerous mutations, including an insertion, deletion, and substitution, which rendered them inactive. They concluded that there are 2 expressed genes, but

only 1 gene product and that both expressed genes are located on chromosome 11. Human adrenodoxin and placental ferredoxin cDNAs share an identical sequence, suggesting that they are the same (Mittal et al., 1988).

Chashchin et al. (1986) found that adrenodoxin is identical in sequence to liver ferredoxin (hepatoredoxin). Renal ferredoxin (renodoxin) has similar optic, renal, and immunochemical properties to adrenodoxin, although Maruya et al. (1983) suggested that the 2 have minor differences. Because they identified only 1 protein sequence, Chang et al. (1990) suggested that there is no need to designate ferredoxin according to the tissue origin. By in situ hybridization, Sparkes et al. (1991) refined the assignment of ADX to 11q22 and demonstrated pseudo-genes on 20q11-q12.

[12998] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[12999] Chang, C.-Y.; Wu, D.-A.; Lai, C.-C.; Miller, W. L.; Chung, B.-C. : Cloning and structure of the human adrenodoxin gene. DNA 7: 609-615, 1988. ; and

[13000] Sparkes, R. S.; Klisak, I.; Miller, W. L. : Regional mapping of genes encoding human steroidogenic enzymes:

P450scc to 15q23–q24; adrenodoxin to 11q22; adrenodoxin reductase to 17q24–q2.

[13001] Further studies establishing the function and utilities of FDX1 are found in John Hopkins OMIM database record ID 103260, and in cited publications numbered 4101–410 and 4289–4297 listed in the bibliography section herein–below, which are also hereby incorporated by reference. BCL2–associated Athanogene 3 (BAG3, Accession NM_004281) is another VGAM203 host target gene. BAG3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BAG3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG3 BINDING SITE, designated SEQ ID:10493, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[13002] Another function of VGAM203 is therefore inhibition of BCL2–associated Athanogene 3 (BAG3, Accession NM_004281). Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG3. FLJ21369 (Accession NM_024802) is another VGAM203 host target gene.

FLJ21369 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21369, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21369 BINDING SITE, designated SEQ ID:24183, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[13003] Another function of VGAM203 is therefore inhibition of FLJ21369 (Accession NM_024802). Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21369. MGC19556 (Accession NM_033551) is another VGAM203 host target gene. MGC19556 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC19556, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC19556 BINDING SITE, designated SEQ ID:27311, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[13004] Another function of VGAM203 is therefore inhibition of MGC19556 (Accession NM_033551). Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC19556. LOC90632 (Accession XM_033067) is another VGAM203 host target gene. LOC90632 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90632 BINDING SITE, designated SEQ ID:31828, to the nucleotide sequence of VGAM203 RNA, herein designated VGAM RNA, also designated SEQ ID:2914.

[13005] Another function of VGAM203 is therefore inhibition of LOC90632 (Accession XM_033067). Accordingly, utilities of VGAM203 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90632. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 204 (VGAM204) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[13006] VGAM204 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM204 was detected is described hereinabove with reference to Figs. 1–8.

[13007] VGAM204 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13008] VGAM204 gene encodes a VGAM204 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM204 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM204 precursor RNA is designated SEQ ID:190, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:190 is located at position 271598 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13009] VGAM204 precursor RNA folds onto itself, forming

VGAM204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13010] An enzyme complex designated DICER COMPLEX, `dices` the VGAM204 folded precursor RNA into VGAM204 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM204 RNA is designated SEQ ID:2915, and is provided hereinbelow with reference to the sequence listing part.

[13011] VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM204 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13012] VGAM204 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM204 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM204 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13013] The complementary binding of VGAM204 RNA, herein designated VGAM RNA, to host target binding sites on VGAM204 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM204 host target RNA into VGAM204 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13014] It is appreciated that VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM204 host target genes. The mRNA of each one of this plurality of VGAM204 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM204 RNA, herein designated VGAM RNA, and which when bound by VGAM204 RNA causes inhibition of translation of respective one or more VGAM204 host target proteins.

[13015] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM204 gene, herein designated VGAM GENE, on one or more VGAM204 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13016] It is yet further appreciated that a function of VGAM204 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM204 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM204 correlate with, and may be deduced from, the identity of the host

target genes which VGAM204 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [13017] Nucleotide sequences of the VGAM204 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM204 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM204 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM204 are further described hereinbelow with reference to Table 1.
- [13018] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM204 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM204 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [13019] As mentioned hereinabove with reference to Fig. 1, a function of VGAM204 gene, herein designated VGAM is inhibition of expression of VGAM204 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM204 correlate with, and may be deduced from, the identity of the target genes which VGAM204

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13020] Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM_014271) is a VGAM204 host target gene. IL1RAPL1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IL1RAPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RAPL1 BINDING SITE, designated SEQ ID:15554, to the nucleotide sequence of VGAM204 RNA, herein designated VGAM RNA, also designated SEQ ID:2915.

[13021] A function of VGAM204 is therefore inhibition of Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM_014271). Accordingly, utilities of VGAM204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1RAPL1. LOC197322 (Accession XM_117012) is another VGAM204 host target gene. LOC197322 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC197322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197322 BINDING SITE, designated SEQ ID:43204, to the nucleotide sequence of VGAM204 RNA, herein designated VGAM RNA, also designated SEQ ID:2915.

[13022] Another function of VGAM204 is therefore inhibition of LOC197322 (Accession XM_117012). Accordingly, utilities of VGAM204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197322. LOC51313 (Accession NM_016613) is another VGAM204 host target gene. LOC51313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51313 BINDING SITE, designated SEQ ID:18722, to the nucleotide sequence of VGAM204 RNA, herein designated VGAM RNA, also designated SEQ ID:2915.

[13023] Another function of VGAM204 is therefore inhibition of LOC51313 (Accession NM_016613). Accordingly, utilities of VGAM204 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC51313. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 205 (VGAM205) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13024] VGAM205 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM205 was detected is described hereinabove with reference to Figs. 1–8.

[13025] VGAM205 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13026] VGAM205 gene encodes a VGAM205 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM205 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM205 precursor RNA is designated SEQ ID:191, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:191 is located at position 53165 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13027] VGAM205 precursor RNA folds onto itself, forming VGAM205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13028] An enzyme complex designated DICER COMPLEX, `dices` the VGAM205 folded precursor RNA into VGAM205 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM205 RNA is designated SEQ ID:2916, and is provided hereinbelow with reference to the sequence

listing part.

[13029] VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM205 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13030] VGAM205 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM205 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM205 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13031] The complementary binding of VGAM205 RNA, herein designated VGAM RNA, to host target binding sites on VGAM205 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM205 host target RNA into VGAM205 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13032] It is appreciated that VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM205 host target genes. The mRNA of each one of this plurality of VGAM205 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM205 RNA, herein designated VGAM

RNA, and which when bound by VGAM205 RNA causes inhibition of translation of respective one or more VGAM205 host target proteins.

[13033] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM205 gene, herein designated VGAM GENE, on one or more VGAM205 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13034] It is yet further appreciated that a function of VGAM205 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM205 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM205 correlate with, and may be deduced from, the identity of the host target genes which VGAM205 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13035] Nucleotide sequences of the VGAM205 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM205 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM205 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM205 are further described hereinbelow with reference to Table 1.

[13036] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM205 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM205 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13037] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM205 gene, herein designated VGAM is inhibition of expression of VGAM205 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM205 correlate with, and may be deduced from, the identity of the target genes which VGAM205 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13038] Like-glycosyltransferase (LARGE, Accession NM_004737) is a VGAM205 host target gene. LARGE BINDING SITE1 and LARGE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LARGE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LARGE BINDING SITE1 and LARGE BINDING SITE2, designated SEQ ID:11128 and SEQ ID:28600 respectively, to the nucleotide sequence of VGAM205 RNA, herein designated VGAM RNA, also designated SEQ ID:2916.

[13039] A function of VGAM205 is therefore inhibition of Like-glycosyltransferase (LARGE, Accession NM_004737), a gene which is a member of the N-acetylglucosaminyltransferase family. Accordingly, utilities

of VGAM205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LARGE. The function of LARGE has been established by previous studies. Peyrard et al. (1999) investigated the gene content of a segment of 22q12.3–q13.1 that had been shown to contain meningioma-related genes (OMIM Ref. No. 156100) on the basis of studies of deletions. They characterized a new member of the N-acetylglucosaminyltransferase gene family, which they designated the LARGE gene. The LARGE gene spans more than 664 kb of genomic DNA, making it the fifth largest in the human genome, after dystrophin (DMD; 300377), with 2.3 Mb; DCC (OMIM Ref. No. 120470), with 1.4 Mb; GRM8 (OMIM Ref. No. 601116), with 1 Mb; and utrophin (UTRN; 128240), with 900 kb. The LARGE gene contains 16 exons (4,326-bp cDNA) and has an exon content of less than 0.66%, which is similar to the exon content of the DMD gene (0.6%). The chromosomal segment of 22q containing the LARGE gene is apparently poor in genes. By fluorescence in situ hybridization, Peyrard et al. (1999) mapped the mouse Large gene to 8C1 in a region of conserved synteny with 22q12.3–q13.1. The expression pattern of the human and mouse LARGE orthologs is similar. Both

genes are expressed ubiquitously, consistent with their function as housekeeping genes. These genes are also evolutionarily well conserved, as Peyrard et al. (1999) identified an ortholog in *C. elegans* encoding a polypeptide that is 33% identical with the human protein. Michele et al. (2002) demonstrated in both muscle-eye-brain disease (OMIM Ref. No. 253280) and Fukuyama congenital muscular dystrophy (FCMD; 253800) patients that alpha-dystroglycan is expressed at the muscle membrane, but similar hypoglycosylation in the diseases directly abolishes binding activity of dystroglycan for the ligands laminin (see OMIM Ref. No. 150240), neurexin (see OMIM Ref. No. 600565), and agrin (OMIM Ref. No. 103320). Michele et al. (2002) showed that this posttranslational biochemical and functional disruption of alpha-dystroglycan is recapitulated in the muscle and central nervous system of *myd* mice. Michele et al. (2002) demonstrated that *myd* mice have abnormal neuronal migration in the cerebral cortex, cerebellum, and hippocampus, and show disruption of the basal lamina. In addition, *myd* mice reveal that dystroglycan targets proteins to functional sites in brain through its interactions with extracellular matrix proteins. Michele et al. (2002) suggested

that at least 3 mammalian genes function within a convergent posttranslational processing pathway during the biosynthesis of dystroglycan and that abnormal dystroglycan–ligand interactions underlie the pathogenic mechanism of muscular dystrophy with brain abnormalities. Animal model experiments lend further support to the function of LARGE. Michele et al. (2002) demonstrated in both muscle–eye–brain disease (OMIM Ref. No. 253280) and Fukuyama congenital muscular dystrophy (FCMD; 253800) patients that alpha–dystroglycan is expressed at the muscle membrane, but similar hypoglycosylation in the diseases directly abolishes binding activity of dystroglycan for the ligands laminin (see OMIM Ref. No. 150240), neurexin (see OMIM Ref. No. 600565), and agrin (OMIM Ref. No. 103320). Michele et al. (2002) showed that this posttranslational biochemical and functional disruption of alpha–dystroglycan is recapitulated in the muscle and central nervous system of *myd* mice. Michele et al. (2002) demonstrated that *myd* mice have abnormal neuronal migration in the cerebral cortex, cerebellum, and hippocampus, and show disruption of the basal lamina. In addition, *myd* mice reveal that dystroglycan targets proteins to functional sites in brain through its interactions with ex–

tracellular matrix proteins. Michele et al. (2002) suggested that at least 3 mammalian genes function within a convergent posttranslational processing pathway during the biosynthesis of dystroglycan and that abnormal dystroglycan–ligand interactions underlie the pathogenic mechanism of muscular dystrophy with brain abnormalities.

[13040] It is appreciated that the abovementioned animal model for LARGE is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13041] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13042] Grewal, P. K.; Holzfeind, P. J.; Bittner, R. E.; Hewitt, J. E. : Mutant glycosyltransferase and altered glycosylation of alpha-dystroglycan in the myodystrophy mouse. *Nature Genet.* 28: 151–154, 2001. ; and

[13043] Michele, D. E.; Barresi, R.; Kanagawa, M.; Saito, F.; Cohn, R. D.; Satz, J. S.; Dollar, J.; Nishino, I.; Kelley, R. I.; Somer, H.; Straub, V.; Mathews, K. D.; Moore, S. A.; Campbell, K.

[13044] Further studies establishing the function and utilities of LARGE are found in John Hopkins OMIM database record ID 603590, and in cited publications numbered 1271 and

5843 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0895 (Accession XM_166573) is another VGAM205 host target gene. KIAA0895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0895 BINDING SITE, designated SEQ ID:44545, to the nucleotide sequence of VGAM205 RNA, herein designated VGAM RNA, also designated SEQ ID:2916.

[13045] Another function of VGAM205 is therefore inhibition of KIAA0895 (Accession XM_166573). Accordingly, utilities of VGAM205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0895. MGC13102 (Accession NM_032323) is another VGAM205 host target gene. MGC13102 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

MGC13102 BINDING SITE, designated SEQ ID:26133, to the nucleotide sequence of VGAM205 RNA, herein designated VGAM RNA, also designated SEQ ID:2916.

[13046] Another function of VGAM205 is therefore inhibition of MGC13102 (Accession NM_032323). Accordingly, utilities of VGAM205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13102. SCDGF-B (Accession NM_033135) is another VGAM205 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:26981 and SEQ ID:24879 respectively, to the nucleotide sequence of VGAM205 RNA, herein designated VGAM RNA, also designated SEQ ID:2916.

[13047] Another function of VGAM205 is therefore inhibition of SCDGF-B (Accession NM_033135). Accordingly, utilities of VGAM205 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCDGF-B.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 206 (VGAM206) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13048] VGAM206 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM206 was detected is described hereinabove with reference to Figs. 1–8.

[13049] VGAM206 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13050] VGAM206 gene encodes a VGAM206 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM206 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM206 precursor RNA is designated SEQ ID:192, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:192 is

located at position 273179 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13051] VGAM206 precursor RNA folds onto itself, forming VGAM206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13052] An enzyme complex designated DICER COMPLEX, `dices` the VGAM206 folded precursor RNA into VGAM206 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM206 RNA is designated SEQ ID:2917, and is provided hereinbelow with reference to the sequence listing part.

[13053] VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM206 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13054] VGAM206 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM206 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM206 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[13055] The complementary binding of VGAM206 RNA, herein designated VGAM RNA, to host target binding sites on VGAM206 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM206 host target RNA into VGAM206 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13056] It is appreciated that VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM206 host target genes. The mRNA of each one of this plurality of VGAM206 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM206 RNA, herein designated VGAM RNA, and which when bound by VGAM206 RNA causes in-

hibition of translation of respective one or more VGAM206 host target proteins.

[13057] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM206 gene, herein designated VGAM GENE, on one or more VGAM206 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13058] It is yet further appreciated that a function of VGAM206 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM206 include diagnosis, prevention and

treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM206 correlate with, and may be deduced from, the identity of the host target genes which VGAM206 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [13059] Nucleotide sequences of the VGAM206 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM206 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM206 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM206 are further described hereinbelow with reference to Table 1.
- [13060] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM206 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM206 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [13061] As mentioned hereinabove with reference to Fig. 1, a function of VGAM206 gene, herein designated VGAM is

inhibition of expression of VGAM206 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM206 correlate with, and may be deduced from, the identity of the target genes which VGAM206 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13062] Acid Phosphatase, Testicular (ACPT, Accession NM_080789) is a VGAM206 host target gene. ACPT BINDING SITE1 and ACPT BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ACPT, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACPT BINDING SITE1 and ACPT BINDING SITE2, designated SEQ ID:28044 and SEQ ID:28047 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13063] A function of VGAM206 is therefore inhibition of Acid Phosphatase, Testicular (ACPT, Accession NM_080789). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACPT. V-akt Murine Thymoma Viral Onco-

gene Homolog 1 (AKT1, Accession NM_005163) is another VGAM206 host target gene. AKT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKT1 BINDING SITE, designated SEQ ID:11655, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13064] Another function of VGAM206 is therefore inhibition of V-akt Murine Thymoma Viral Oncogene Homolog 1 (AKT1, Accession NM_005163), a gene which Serine-threonine protein kinase. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKT1. The function of AKT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM188.UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Accession NM_014256) is another VGAM206 host target gene. B3GNT3 BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by B3GNT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B3GNT3 BINDING SITE, designated SEQ ID:15532, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13065] Another function of VGAM206 is therefore inhibition of UDP-GlcNAc:betaGal Beta-1,3-N-acetylglucosaminyltransferase 3 (B3GNT3, Accession NM_014256). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B3GNT3. Beta-site APP-cleaving Enzyme (BACE, Accession NM_138971) is another VGAM206 host target gene. BACE BINDING SITE1 and BACE BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BACE, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACE BINDING SITE1 and BACE BINDING SITE2, designated SEQ ID:29088 and SEQ ID:14420 respectively,

to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13066] Another function of VGAM206 is therefore inhibition of Beta-site APP-cleaving Enzyme (BACE, Accession NM_138971), a gene which is responsible for the proteolytic processing of the amyloid precursor protein. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACE. The function of BACE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. CD34 Antigen (CD34, Accession NM_001773) is another VGAM206 host target gene. CD34 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD34 BINDING SITE, designated SEQ ID:7536, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13067] Another function of VGAM206 is therefore inhibition of CD34 Antigen (CD34, Accession NM_001773), a gene

which is a monomeric cell surface antigen that is selectively expressed on human hematopoietic progenitor cells. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD34. The function of CD34 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. CD53 Antigen (CD53, Accession NM_000560) is another VGAM206 host target gene. CD53 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD53, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD53 BINDING SITE, designated SEQ ID:6170, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13068] Another function of VGAM206 is therefore inhibition of CD53 Antigen (CD53, Accession NM_000560). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD53. Centromere Protein B, 80kDa (CENPB, Accession XM_045451) is another VGAM206 host target

gene. CENPB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENPB BINDING SITE, designated SEQ ID:34464, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13069] Another function of VGAM206 is therefore inhibition of Centromere Protein B, 80kDa (CENPB, Accession XM_045451), a gene which is the major centromere antigen. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENPB. The function of CENPB has been established by previous studies. The structure and function of the centromere regions of mitotic chromosomes have been of interest to cell biologists, geneticists and rheumatologists. Cell biologists focus on the centromere as both the site of sister chromatid pairing and the site of mitotic spindle attachment. The latter site, the kinetochore, is a trilaminar plaque structure embedded in the chromatin at the surface of the chromosome, as visu-

alized by electron microscopy. Geneticists have been interested in centromeric sequences involved in the control of chromosomal segregation. Rheumatologists became interested in centromere structure when it was observed that centromere compounds are the target of autoimmune responses. Earnshaw et al. (1987) isolated a series of overlapping DNA clones for about 95% of the mRNA that encodes the B centromeric protein. Anticentromere antibodies recognize 3 antigens: CENPA (17 kD; 117139), CENPB (80 kD), and CENPC (140 kD; 117141). CENPB is considered the major centromere antigen since antibody to it is consistently present at high titer in serum positive for anticentromere antibodies. The B protein is the product of a 2.9-kb mRNA that is encoded by a single locus. By optimizing the primer-annealing temperature in a rapid air cycling procedure, Sugimoto et al. (1993) specifically amplified human DNA sequences encoding CENPB and CENPC, without any detectable amplification of highly homologous rodent DNA sequences. Using a panel of rodent/human hybrid DNAs, the human CENPB and CENPC genes were mapped to chromosomes 20 and 12, respectively. By fluorescence in situ hybridization, Seki et al. (1994) assigned the CENPB gene to 20p13.

[13070] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13071] Earnshaw, W. C.; Sullivan, K. F.; Machlin, P. S.; Cooke, C. A.; Kaiser, D. A.; Pollard, T. D.; Rothfield, N. F.; Cleveland, D. W. : Molecular cloning of cDNA for CENP-B, the major human centromere autoantigen. J. Cell Biol. 104: 817-829, 1987. ; and

[13072] Seki, N.; Saito, T.; Kitagawa, K.; Masumoto, H.; Okazaki, T.; Hori, T.-A. : Mapping of the human centromere protein B gene (CENPB) to chromosome 20p13 by fluorescence in situ hybridizat.

[13073] Further studies establishing the function and utilities of CENPB are found in John Hopkins OMIM database record ID 117140, and in cited publications numbered 4671-4673 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.Deleted In Azoospermia (DAZ, Accession NM_004081) is another VGAM206 host target gene. DAZ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of DAZ BINDING SITE, designated SEQ ID:10284, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13074] Another function of VGAM206 is therefore inhibition of Deleted In Azoospermia (DAZ, Accession NM_004081), a gene which may play a role in the germ-cell-specific patterns of RNA splicing and storage. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAZ. The function of DAZ has been established by previous studies. Cooke et al. (1996) postulated that the DAZ gene product may play a role in the germ-cell-specific patterns of RNA splicing and storage. They isolated the mouse homolog of DAZ and mapped it by fluorescence in situ hybridization to chromosome 17 at position 25.6 cM. Cooke et al. (1996) reported that the predicted protein product of the mouse homolog is highly homologous to that of the human gene. By RT-PCR analysis, they established that transcripts occur only in mouse germ cells. Deletions of the azoospermia factors on the Y chromosome long arm are an important cause of male infertility, and they may involve germ cell-specific genes or ubiquitously expressed

genes. Foresta et al. (2001) hypothesized that microdeletions involving genes specifically expressed in germ cells should not alter Sertoli cell function. To examine this, they evaluated the testicular hormonal function in infertile patients affected by severe testiculopathies with and without Yq microdeletions, with particular emphasis on Sertoli cell function. They studied 102 well-characterized infertile patients; 27 had Yq microdeletions, and 75 were classified as idiopathic infertiles. Patients with Yq microdeletions had lower FSH (see OMIM Ref. No. 136530) and higher inhibin B (see OMIM Ref. No. 147290) plasma concentrations compared to patients without microdeletions, suggesting that Sertoli cell function in Yq-deleted men is only partially altered. Furthermore, patients with deletions involving germ cell-specific genes had higher concentrations of inhibin B compared to patients with deletions of ubiquitously expressed genes. The authors inferred that a specific alteration of germ cells only partially influences Sertoli cell function. The hormonal status of patients without deletions suggested that in such cases the cause of the spermatogenic defect may have damaged both Sertoli and germ cells. Inhibin B production in patients with Yq deletions was about 70% higher than in nondeleted pa-

tients, and the functional relationship between FSH and inhibin B was normally preserved.

[13075] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13076] Cooke, H. J.; Lee, M.; Kerr, S.; Ruggiu, M. : A murine homologue of the human DAZ gene is autosomal and expressed only in male and female gonads. Hum. Molec. Genet. 5: 513–516, 1996. ; and

[13077] Foresta, C.; Bertella, A.; Moro, E.; Roverato, A.; Merico, M.; Ferlin, A. : Sertoli cell function in infertile patients with and without microdeletions of the azoospermia factors on th.

[13078] Further studies establishing the function and utilities of DAZ are found in John Hopkins OMIM database record ID 400003, and in cited publications numbered 8236–8238, 8234, 8239–8242, 8246–8245, 880 and 8826 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.Deleted In Azoospermia-like (DAZL, Accession XM_042839) is another VGAM206 host target gene. DAZL BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DAZL, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAZL BINDING SITE, designated SEQ ID:33800, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13079] Another function of VGAM206 is therefore inhibition of Deleted In Azoospermia-like (DAZL, Accession XM_042839), a gene which may be essential for gametogenesis. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAZL. The function of DAZL has been established by previous studies. Yen et al. (1996) reported the isolation of a human gene homolog of the mouse Dazla gene by screening of a testis-specific library with a DAZ cDNA clone. The gene they isolated contained only 1 of 7 repeats found in DAZ, showed a high degree of homology to the mouse Dazla gene, and mapped to chromosome 3p24. RBM and DAZ/SPGY are 2 families of genes located on the Y chromosome that encode proteins containing RNA-binding motifs, and both have been described as candidate human spermatogenesis genes. Neither gene family had been shown to be es-

essential for spermatogenesis in human males, but a Dazla homolog in *Drosophila* is essential for spermatogenesis (Eberhart et al., 1996). With a polyclonal antibody raised in rabbits against Dazla and with knockout technology in mice, Rugglu et al. (1997) demonstrated that the Dazla protein is cytoplasmic in male and female germ cells, unlike the nuclear RBM protein. Disruption of the Dazla gene led to loss of germ cells and complete absence of gamete production, demonstrating that Dazla is essential for the differentiation of germ cells.

[13080] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13081] Yen, P. H.; Chai, N. N.; Salido, E. C. : The human autosomal gene DAZLA: testis specificity and a candidate for male infertility. *Hum. Molec. Genet.* 5: 2013–2017, 1996. ; and

[13082] Rugglu, M.; Speed, R.; Taggart, M.; McKay, S. J.; Kilanowski, F.; Saunders, P.; Derin, J.; Cooke, H. J. : The mouse Dazla gene encodes a cytoplasmic protein essential for gametogenesis.

[13083] Further studies establishing the function and utilities of DAZL are found in John Hopkins OMIM database record ID

601486, and in cited publications numbered 8236–683 and 8245–6835 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Diacylglycerol O–acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM_032564) is another VGAM206 host target gene. DGAT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DGAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DGAT2 BINDING SITE, designated SEQ ID:26294, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13084] Another function of VGAM206 is therefore inhibition of Diacylglycerol O–acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM_032564). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGAT2. Discs, Large (Drosophila) Homolog 4 (DLG4, Accession NM_001365) is another VGAM206 host target gene. DLG4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DLG4, corre–

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLG4 BINDING SITE, designated SEQ ID:7047, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13085] Another function of VGAM206 is therefore inhibition of Discs, Large (Drosophila) Homolog 4 (DLG4, Accession NM_001365), a gene which is a membrane-associated guanylate kinase and may intervene in synaptogenesis. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLG4. The function of DLG4 has been established by previous studies. Neuregulins and their receptors, the ERBB protein tyrosine kinases, are essential for neuronal development, but their functions in the adult central nervous system are unknown. Huang et al. (2000) reported that ERBB4 (OMIM Ref. No. 600543) is enriched in the postsynaptic density and associates with PSD95. Heterologous expression of PSD95 enhanced NRG (OMIM Ref. No. 142445) activation of ERBB4 and MAP kinase (see OMIM Ref. No. 176948). Conversely, inhibiting expression of PSD95 in neurons attenuated NRG-mediated activation

of MAP kinase. PSD95 formed a ternary complex with 2 molecules of ERBB4, suggesting that PSD95 facilitates ERBB4 dimerization. Finally, NRG suppressed induction of long-term potentiation in the hippocampal CA1 region without affecting basal synaptic transmission. Thus, NRG signaling may be synaptic and regulated by PSD95. Huang et al. (2000) concluded that a role of NRG signaling in the adult central nervous system may be modulation of synaptic plasticity. El-Husseini et al. (2002) identified palmitate cycling on PSD95 at the synapse and found that palmitate turnover on PSD95 is regulated by glutamate receptor activity. Acutely blocking palmitoylation dispersed synaptic clusters of PSD95 and caused a selective loss of synaptic AMPA receptors (e.g., GRIA1; 138248). The authors also found that rapid glutamate-mediated AMPA receptor internalization requires depalmitoylation of PSD95. In a nonneuronal model system, clustering of PSD95, stargazin (OMIM Ref. No. 602911), and AMPA receptors was also regulated by ongoing palmitoylation of PSD95 at the plasma membrane. El-Husseini et al. (2002) concluded that palmitate cycling on PSD95 can regulate synaptic strength and activity-dependent plasticity.

[13086] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [13087] Huang, Y. Z.; Won, S.; Ali, D. W.; Wang, Q.; Tanowitz, M.; Du, Q. S.; Pelkey, K. A.; Yang, D. J.; Xiong, W. C.; Salter, M. W.; Mei, L. : Regulation of neuregulin signaling by PSD-95 interacting with ErbB4 at CNS synapses. *Neuron* 26: 443–455, 2000. ; and
- [13088] El-Husseini, A. E.-D.; Schnell, E.; Dakoji, S.; Sweeney, N.; Zhou, Q.; Prange, O.; Gauthier-Campbell, C.; Aguilera-Moreno, A.; Nicoll, R. A.; Bredt, D. S. : Synaptic strength regulated.
- [13089] Further studies establishing the function and utilities of DLG4 are found in John Hopkins OMIM database record ID 602887, and in cited publications numbered 5327–532 and 11573–5334 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Egl Nine Homolog 3 (*C. elegans*) (EGLN3, Accession NM_022073) is another VGAM206 host target gene. EGLN3 BINDING SITE1 and EGLN3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by EGLN3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of EGLN3 BINDING SITE1 and EGLN3 BINDING SITE2, designated SEQ ID:22619 and SEQ ID:27198 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13090] Another function of VGAM206 is therefore inhibition of Egl Nine Homolog 3 (*C. elegans*) (EGLN3, Accession NM_022073), a gene which is an essential component of the pathway. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN3. The function of EGLN3 has been established by previous studies. In cultured mammalian cells, Bruick and McKnight (2001) found that the inappropriate accumulation of HIF caused by forced expression of the HIF1-alpha subunit under normoxic conditions was attenuated by coexpression of HPH. Suppression of HPH in cultured *Drosophila melanogaster* cells by RNA interference resulted in elevated expression of the hypoxia-inducible gene LDH (see OMIM Ref. No. 150000) under normoxic conditions. Bruick and McKnight (2001) concluded that HPH is an essential component of the pathway through which cells sense oxygen. HIF is a transcriptional complex that plays a central role in mam-

malian oxygen homeostasis. Posttranslational modification by prolyl hydroxylation is a key regulatory event that targets HIF- α (HIF1; 603348) subunits for proteasomal destruction via the von Hippel-Lindau (VHL; 193300) ubiquitylation complex. Epstein et al. (2001) defined a conserved HIF-VHL-prolyl hydroxylase pathway in *C. elegans* and identified Egl9 as a dioxygenase that regulates HIF by prolyl hydroxylation. In mammalian cells, they showed that the HIF-prolyl hydroxylases are represented by 3 proteins with a conserved 2-histidine-1-carboxylate iron coordination motif at the catalytic site. The genes encoding these proteins were cloned and termed PHD1 (OMIM Ref. No. 606424), PHD2 (OMIM Ref. No. 606425), and PHD3 by the authors. Direct modulation of recombinant enzyme activity by graded hypoxia, iron chelation, and cobaltous ions mirrored the characteristics of HIF induction in vivo, fulfilling requirements for these enzymes being oxygen sensors that regulate HIF.

[13091] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13092] Bruick, R. K.; McKnight, S. L. : A conserved family of prolyl-4-hydroxylases that modify HIF. *Science* 294:

1337–1340, 2001. ; and

[13093] Epstein, A. C. R.; Gleadle, J. M.; McNeill, L. A.; Hewitson, K. S.; O'Rourke, J.; Mole, D. R.; Mukherji, M.; Metzen, E.; Wilson, M. I.; Dhanda, A.; Tian, Y.-M.; Masson, N.; Hamilton, D.

[13094] Further studies establishing the function and utilities of EGLN3 are found in John Hopkins OMIM database record ID 606426, and in cited publications numbered 4543–4544 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fucosyltransferase 9 (alpha (1,3) Fucosyltransferase) (FUT9, Accession XM_042167) is another VGAM206 host target gene. FUT9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT9 BINDING SITE, designated SEQ ID:33700, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13095] Another function of VGAM206 is therefore inhibition of Fucosyltransferase 9 (alpha (1,3) Fucosyltransferase)

(FUT9, Accession XM_042167), a gene which catalyzes alpha-1,3 glycosidic linkages. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT9. The function of FUT9 has been established by previous studies. FUT9 is one of several alpha-3-fucosyltransferases that can catalyze the last step in the biosynthesis of Lewis antigen, the addition of a fucose to precursor polysaccharides. FUT9 synthesizes the LeX oligosaccharide, which is expressed in organ buds progressing in mesenchyma during human embryogenesis.

[13096] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13097] Cailleau-Thomas, A.; Coullin, P.; Candelier, J.-J.; Balanzino, L.; Mennesson, B.; Oriol, R.; Mollicone, R. : FUT4 and FUT9 genes are expressed early in human embryogenesis. *Glycobiology* 10: 789-802, 2000. ; and

[13098] Kaneko, M.; Kudo, T.; Iwasaki, H.; Ikehara, Y.; Nishihara, S.; Nakagawa, S.; Sasaki, K.; Shiina, T.; Inoko, H.; Saitou, N.; Narimatsu, H. : Alpha-1,3-fucosyltransferase (sic) IX (Fuc-T.

[13099] Further studies establishing the function and utilities of

FUT9 are found in John Hopkins OMIM database record ID 606865, and in cited publications numbered 83 and 5581–5582 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.UDP–N–acetyl–alpha–D–galactosamine:polypeptide N–acetylgalactosaminyltransferase 2 (GalNAc–T2) (GALNT2, Accession NM_004481) is another VGAM206 host target gene. GALNT2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GALNT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT2 BINDING SITE, designated SEQ ID:10798, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13100] Another function of VGAM206 is therefore inhibition of UDP–N–acetyl–alpha–D–galactosamine:polypeptide N–acetylgalactosaminyltransferase 2 (GalNAc–T2) (GALNT2, Accession NM_004481), a gene which catalyzes the initial reaction in o–linked oligosaccharide biosynthesis. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associ–

ated with GALNT2. The function of GALNT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM187. G Protein-coupled Receptor 63 (GPR63, Accession NM_030784) is another VGAM206 host target gene. GPR63 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPR63, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPR63 BINDING SITE, designated SEQ ID:25079, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13101] Another function of VGAM206 is therefore inhibition of G Protein-coupled Receptor 63 (GPR63, Accession NM_030784), a gene which transduces extracellular signals through heterotrimeric G proteins. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPR63. The function of GPR63 has been established by previous studies. Using degenerate primers designed from sequence conserved between *Xenopus* and mouse PSP24

homologs, Kawasaki et al. (2000) cloned GPR63, which they called PSP24B, by PCR followed by RACE using human brain mRNA as template. The deduced 419–amino acid protein shares 57% identity with *Xenopus* PSP24 and 92% identity with the mouse homolog. Lee et al. (2001) identified GPR63 within a human genomic DNA library using GPR61 (OMIM Ref. No. 606916) as probe. Primers to the intronless sequence were synthesized, and GPR63 cDNA was amplified by PCR and cloned. Northern blot analysis revealed expression of a single 6.8–kb transcript in various brain regions, with stronger expression in caudate and thalamus, and fainter expression in hypothalamus and midbrain. Kawasaki et al. (2000) cloned mouse *Gpr63*, which they called mPSP24B, by screening a mouse genomic library with the cDNA fragment of *Xenopus* PSP24. The 6.0–kb mouse transcript was expressed almost exclusively in brain. In situ hybridization of mouse brain sections revealed expression in neuronal cells such as olfactory mitral cells, cortical neurons, hippocampal pyramidal cells, and Purkinje cells in the cerebellum. Kawasaki et al. (2000) noted that *Xenopus* PSP24 was originally identified as a lysophosphatidic acid receptor (LPA). Functional analysis of mouse *Gpr63* transfected into

a rat hepatoma cell line suggested that the mouse protein does not function as an LPA receptor.

[13102] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13103] Kawasaki, Y.; Kume, K.; Nakade, S.; Haga, H.; Izumi, T.; Shimizu, T. : Brain-specific expression of novel G-protein-coupled receptors, with homologies to Xenopus PSP24 and human GPR45. Biochem. Biophys. Res. Commun. 276: 952-956, 2000. ; and

[13104] Lee, D. K.; George, S. R.; Cheng, R.; Nguyen, T.; Liu, Y.; Brown, M.; Lynch, K. R.; O'Dowd, B. F. : Identification of four novel human G protein-coupled receptors expressed in the brain.

[13105] Further studies establishing the function and utilities of GPR63 are found in John Hopkins OMIM database record ID 606915, and in cited publications numbered 5501-5503 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843) is another VGAM206 host target gene. GRM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GRM6,

corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GRM6 BINDING SITE, designated SEQ ID:6512, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13106] Another function of VGAM206 is therefore inhibition of Glutamate Receptor, Metabotropic 6 (GRM6, Accession NM_000843). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GRM6. Guanylate Cyclase 1, Soluble, Alpha 3 (GUCY1A3, Accession XM_032838) is another VGAM206 host target gene. GUCY1A3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GUCY1A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GUCY1A3 BINDING SITE, designated SEQ ID:31780, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13107] Another function of VGAM206 is therefore inhibition of Guanylate Cyclase 1, Soluble, Alpha 3 (GUCY1A3, Acces-

sion XM_032838), a gene which is alpha 1 (alpha 3) subunit of soluble guanylate cyclase and forms a heterodimer with GUCY1B3 that converts GTP to cGMP. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GUCY1A3. The function of GUCY1A3 has been established by previous studies. Cyclic GMP (cGMP) plays an important role as an intracellular messenger. The diverse array of its functions includes a central role in phototransduction and in platelet function. Synthesis of cGMP is catalyzed by guanylyl cyclase which exists in soluble and particulate isoforms. Soluble guanylyl cyclase is a dimer composed of a large (alpha) and a small (beta) subunit. Both subunits, alpha-3 and beta-3, were cloned from human brain by Giuli et al. (1992). They found that the alpha-3 and beta-3 subunits are of 82 kD and 70 kD, respectively. Giuli et al. (1993) used the cDNAs coding for these 2 subunits to identify the chromosomal location of the corresponding genes by in situ hybridization. Each probe gave a strong specific signal on chromosome 4 at the 4q31.3-q33 region, with the maximal signal in the 4q32 band. The colocalization of these genes may be related to the coordinated regulation of their expression.

- [13108] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [13109] Giuili, G.; Roechel, N.; Scholl, U.; Mattei, M.-G.; Guellaen, G. : Colocalization of the genes coding for the alpha-3 and beta-3 subunits of soluble guanylyl cyclase to human chromosome 4 at q31.3-q33. Hum. Genet. 91: 257-260, 1993. ; and
- [13110] Giuili, G.; Scholl, U.; Bulle, F.; Guellaen, G. : Molecular cloning of the cDNAs coding for the two subunits of soluble guanylyl cyclase from human brain. FEBS Lett. 304: 83-88, 1992.
- [13111] Further studies establishing the function and utilities of GUCY1A3 are found in John Hopkins OMIM database record ID 139396, and in cited publications numbered 298 and 3571 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glycophorin A (includes MN blood group) (GYPA, Accession XM_113439) is another VGAM206 host target gene. GYPA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GYPA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of GYPA BINDING SITE, designated SEQ ID:42264, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13112] Another function of VGAM206 is therefore inhibition of Glycophorin A (includes MN blood group) (GYPA, Accession XM_113439), a gene which determines the M or N blood group. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GYPA. The function of GYPA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM145. Homeo Box A7 (HOXA7, Accession NM_006896) is another VGAM206 host target gene. HOXA7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXA7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXA7 BINDING SITE, designated SEQ ID:13772, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13113] Another function of VGAM206 is therefore inhibition of Homeo Box A7 (HOXA7, Accession NM_006896), a gene which provides cells with specific positional identities on the anterior–posterior axis. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXA7. The function of HOXA7 has been established by previous studies. The homeotic genes, whose products serve as determinants of embryonic cell fate, are expressed in a series of different but partially overlapping domains that extend along the anterior–posterior (A–P) axis of the embryo. The Hox genes share a 180–bp homeo box, which encodes a 60–amino acid homeodomain that binds specifically to DNA. There are 4 Hox gene clusters: HOXA (formerly HOX1) on chromosome 7, HOXB (formerly HOX2) on chromosome 17, HOXC (formerly HOX3) on chromosome 12, and HOXD (formerly HOX4) on chromosome 2. By sequence comparison, the genes of each cluster are assigned to 1 of 13 groups. The order of the HOX genes along the chromosome reflects where they are expressed along the body axis. This principle is followed in homeo box gene nomenclature. For a review of homeo box gene nomenclature, see Scott (1992). The homeo box is a

180-bp DNA sequence conserved in *Drosophila* homeotic genes which regulate early development (review by Gehring, 1985). These DNA sequences are present in open reading frames and have been identified in *Drosophila* and *Xenopus* embryos. They share structural features with genes encoding some DNA-binding proteins. Homologous homeo box sequences have been detected in species ranging from insects and annelids to vertebrates. The high degree of sequence conservation (70 to 90%) suggests a common role in embryonic development.

Schughart et al. (1989) pointed to evidence of duplication of large genomic regions during evolution of the mouse homeo box genes. The findings were considered consistent with the hypothesis of Ohno (1970) that during vertebrate evolution duplications of the entire genome occurred. Such are likely to be less deleterious than duplications of individual chromosomes. Ferguson-Smith et al. (1989) showed that the sequence of the HOX1 gene has 100% identity to the deduced amino acid sequence of the mouse HOX1.4 homeo box. They detected no RFLPs with the 14-kD clone, which was devoid of any moderately repetitive DNA sequences. This implied an inability of this region to tolerate change in sequence, consistent with a

function highly conserved throughout evolution. Animal model experiments lend further support to the function of HOXA7. As reviewed by Gaunt and Singh (1990), in both the mouse and *Drosophila*, Antennapedia-like homeobox-containing genes (homeogenes) display a strict correspondence between the order of genes (3-prime to 5-prime) along the chromosome and the order of their expression domains (anterior to posterior) in the developing embryo. Gaunt and Singh (1990) suggested that this and other points of similarity indicate that the 2 species use a common mechanism of chromosomal imprinting in order to retain cellular memory of homeogene expression patterns throughout embryonic development. The 'open for transcription' model suggests that imprinting is a matter of open and closed chromatin, the molecular nature of which is not clear. It is possible that a clue to the mechanism of memory used within the homeogene complex, at least in *Drosophila*, is provided by the *Drosophila* mutant 'Polycomb' (Pc). The product of the Pc gene, which presumably has a homolog in man, appears to act as a repressor of 'posterior' genes in anterior segments. Thus, it may be involved in restricting the state of 'openness' of the homeotic gene complex.

- [13114] It is appreciated that the abovementioned animal model for HOXA7 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.
- [13115] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [13116] Schughart, K.; Kappen, C.; Ruddle, F. H. : Duplication of large genomic regions during the evolution of vertebrate homeobox genes. Proc. Nat. Acad. Sci. 86: 7067–7071, 1989. ; and
- [13117] Scott, M. P. : Vertebrate homeobox gene nomenclature. (Letter) Cell 71: 551–553, 1992.
- [13118] Further studies establishing the function and utilities of HOXA7 are found in John Hopkins OMIM database record ID 142950, and in cited publications numbered 5207–5221 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Homeo Box C4 (HOXC4, Accession NM_014620) is another VGAM206 host target gene. HOXC4 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HOXC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXC4 BINDING SITE, designated SEQ ID:15975, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13119] Another function of VGAM206 is therefore inhibition of Homeo Box C4 (HOXC4, Accession NM_014620), a gene which is part of a developmental regulatory system that provides cells with specific positional identities on the anterior-posterior axis. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXC4. The function of HOXC4 has been established by previous studies. As reviewed by Acampora et al. (1989), the homeo box region 3, which maps to 12q12-q13, contains at least 7 homeo boxes in 160 kb of DNA. HOX3A is homologous to mouse Hox-3.1; HOX3B to mouse Hox-3.2; HOX3C to mouse Hox-6.1, and HOX3D to mouse Hox-6.2. The order of genes, from 5-prime to 3-prime, is HOX3G, HOX3F, HOX3B, HOX3A, HOX3C, HOX3D, HOX3E (Acampora et al., 1989). Masuda et al. (1991) mapped the feline equivalent to chromosome B4, which shares syntenic homology with human chromosome 12 and mouse chromosome 15. This

gene is also called HOXC8; see HOXC9 (OMIM Ref. No. 142971). Yueh et al. (1998) showed that overexpression of a Hoxc8 transgene causes cartilage defects whose severity depends on transgene dosage. The abnormal cartilage is characterized by an accumulation of proliferating chondrocytes and reduced maturation. Since Hoxc8 is normally expressed in chondrocytes, these results suggested that Hoxc8 continues to regulate skeletal development well beyond pattern formation in a tissue-specific manner, presumably by controlling the progression of cells along the chondrocyte differentiation pathway. They found that Hoxd4 and Hoxc8 appear to act on chondrocyte differentiation in a similar manner. The protein sequences of the 2 share 67% identity within the homeodomain and 50% in the hexapeptide motif but little similarity in the remaining 70% of the molecules. Isl1, which shares no significant sequence similarities with Hoxc8 or Hoxd4, is not associated with abnormalities of skeletal development, implying that the cartilage abnormalities are specifically induced by HOX genes. The capacity of the HOX genes to regulate cartilage differentiation suggests that they may be involved in human chondrodysplasias or other cartilage disorders.

- [13120] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [13121] Simeone, A.; Pannese, M.; Acampora, D.; D'Esposito, M.; Boncinelli, E. : At least three human homeoboxes on chromosome 12 belong to the same transcription unit. *Nucleic Acids Res.* 16: 5379–5390, 1988. ; and
- [13122] Yueh, Y. G.; Gardner, D. P.; Kappen, C. : Evidence for regulation of cartilage differentiation by the homeobox gene *Hoxc-8*. *Proc. Nat. Acad. Sci.* 95: 9956–9961, 1998.
- [13123] Further studies establishing the function and utilities of *HOXC4* are found in John Hopkins OMIM database record ID 142974, and in cited publications numbered 5223 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. *Hippocalcin-like 1* (*HPCAL1*, Accession NM_134421) is another VGAM206 host target gene. *HPCAL1 BINDING SITE* is *HOST TARGET* binding site found in the 5' untranslated region of mRNA encoded by *HPCAL1*, corresponding to a *HOST TARGET* binding site such as *BINDING SITE I*, *BINDING SITE II* or *BINDING SITE III*. Table 2 illustrates the complementarity of the nucleotide sequences of *HPCAL1 BINDING SITE*, designated SEQ ID:28639, to the nucleotide sequence of

VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13124] Another function of VGAM206 is therefore inhibition of Hippocalcin-like 1 (HPCAL1, Accession NM_134421). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL1. IRTA2 (Accession NM_031281) is another VGAM206 host target gene. IRTA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRTA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRTA2 BINDING SITE, designated SEQ ID:25298, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13125] Another function of VGAM206 is therefore inhibition of IRTA2 (Accession NM_031281), a gene which binds to the γ region of immunoglobulins gamma low affinity receptor. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRTA2. The function of IRTA2 has been established by previous studies. Chromosomal ab-

normalities involving translocation breakpoints at 1q21–q23 are frequent in B–cell non–Hodgkin lymphoma (see OMIM Ref. No. BCL9; 602597) and multiple myeloma (MM; OMIM Ref. No. 254500). By cloning the breakpoints of a (1;14)(q21;q32) chromosomal translocation in the FR4 multiple myeloma cell line, followed by exon trapping and screening a spleen cDNA library, Hatzivassiliou et al. (2001) obtained cDNAs encoding 3 isoforms of IRTA1 (OMIM Ref. No. 605876) and 4 isoforms of IRTA2. The 3 major IRTA2 mRNA isoforms (ITRA2A, ITRA2B, and ITRA2C) each have their own unique 3–prime untranslated region, and the proteins they encode share a common amino acid sequence until residue 560, including a signal peptide and 6 extracellular Ig–type domains. Sequence analysis predicted that IRTA2A is a 759–amino acid secreted glycoprotein with 8 total extracellular Ig–type domains followed by 13 unique, predominantly polar residues at its C terminus. After the common 560 amino acids, IRTA2B has only 32 additional residues, whose hydrophobicity is compatible with its docking to the plasma membrane via a GPI anchor. The 977–amino acid IRTA2C protein shares the first 746 amino acids with IRTA2A. IRTA2C has a total of 9 extracellular Ig–type domains with

8 potential N-linked glycosylation sites; a 23-residue transmembrane region; and a 104-residue cytoplasmic domain with 3 consensus SH2-binding domains, all of which exhibit features of ITIMs (immune-receptor tyrosine-based inhibition motifs) and are encoded by separate exons. The fourth isoform, IRTA2D, encodes a peptide of 152 amino acids. Northern blot analysis detected 2.8-, 4.4-, 5.3-, and 0.6-kb IRTA2 transcripts in lymph node, spleen, bone marrow, and small intestine, with a preponderance of the IRTA2A isoform. In situ hybridization analysis detected IRTA2 expression in tonsillar germinal center centrocytes, but not in centroblasts, as well as in intraepithelial and interfollicular regions. Nakayama et al. (2001) independently cloned IRTA2, which they called BX-MAS1, by representational difference analysis of genes activated by anti-IgM crosslinking of a human B-cell line. The deduced 977-amino acid protein contains 8 ITIMs and 8 potential N-linked glycosylation sites. Northern blot analysis detected a 6.7-kb transcript and a larger transcript between 14- and 17-kb in B cells 24 to 36 hours after activation. Northern blot analysis of tissues detected expression only in spleen. In situ hybridization analysis demonstrated expression of IRTA2 in the mantle zone of

tonsil tissue but not in germinal center cells

[13126] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13127] Hatzivassiliou, G.; Miller, I.; Takizawa, J.; Palanisamy, N.; Rao, P. H.; Iida, S.; Tagawa, S.; Taniwaki, M.; Russo, J.; Neri, A.; Cattoretti, G.; Clynes, R.; Mendelsohn, C.; Chaganti, R. S. K.; Dalla-Favera, R. : IRTA1 and IRTA2, novel immunoglobulin superfamily receptors expressed in B cells and involved in chromosome 1q21 abnormalities in B cell malignancy. *Immunity* 14: 277–289, 2001. ; and

[13128] Nakayama, Y.; Weissman, S. M.; Bothwell, A. L. M. : BX–MAS1 identifies a cluster of homologous genes differentially expressed in B cells. *Biochem. Biophys. Res. Commun.* 285: 830–837, 2001.

[13129] Further studies establishing the function and utilities of IRTA2 are found in John Hopkins OMIM database record ID 605877, and in cited publications numbered 29 and 7008 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Itchy Homolog E3 Ubiquitin Protein Ligase (mouse) (ITCH, Accession NM_031483) is another VGAM206 host target gene. ITCH BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by ITCH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITCH BINDING SITE, designated SEQ ID:25564, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13130] Another function of VGAM206 is therefore inhibition of Itchy Homolog E3 Ubiquitin Protein Ligase (mouse) (ITCH, Accession NM_031483), a gene which accepts ubiquitin from an e2 ubiquitin-conjugating enzyme in the form of a thioester and then directly transfers the ubiquitin to targeted substrates. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITCH. The function of ITCH has been established by previous studies. Using GST pull-down and coimmunoprecipitation experiments, Winberg et al. (2000) demonstrated that ITCH and KIAA0439 (OMIM Ref. No. 606384) form physiologic complexes with the Epstein-Barr virus (EBV) latent membrane protein 2a (LMP2A) in EBV-positive cells. They concluded that the ability of LMP2A to recognize the WW domains of ITCH or KIAA0439 is dependent on the LMP2A PPPPY motifs. Using

chimeric protein analysis, they determined that the N-terminal region of LMP2A is necessary and sufficient for binding to ITCH and that this interaction is not dependent on tyrosine phosphorylation. The authors hypothesized that LMP2A promotes ITCH-mediated ubiquitination of Lyn (OMIM Ref. No. 165120) and Syk (OMIM Ref. No. 600085). With GST pull-down assays and immunoprecipitation assays, Qiu et al. (2000) demonstrated that Itch binds to the N-terminal portion of the Notch (see OMIM Ref. No. 190198) intracellular domain via its WW domains and promotes ubiquitination of Notch through its HECT ubiquitin ligase domain. They hypothesized that Itch may participate in the regulation of immune responses by modifying Notch-mediated signaling. Using transfection experiments, Chen et al. (2001) concluded that ITCH can act as a transcriptional corepressor of p45/NFE2. The interaction between these 2 proteins is modulated through the WW1 domain of ITCH and requires the PY motif of p45/NFE2. In cotransfection assays, they observed that ITCH suppressed transcriptional activation by p45/NFE2. They hypothesized that the erythroid hyperplasia observed in a18H mice (see OMIM Ref. No. Animal Model section) is likely due to the loss of NFE2/ITCH interaction.

Animal model experiments lend further support to the function of ITCH. By analyzing genomic clones from wild-type and mutant mice, Perry et al. (1998) determined that the phenotype of the non-agouti-lethal 18H (a18H) or Itchy mice results from a small inversion that disrupts both the agouti and the Itch genes. The mice develop a spectrum of immunologic diseases not seen in other mice with mutations in agouti. The phenotype includes inflammation of the lung and stomach, hyperplasia of lymphoid and hematopoietic cells, and constant itching in the skin, suggesting that Itch is involved in the regulation of immune response. The inversion in a18H mice appears to produce a null allele of Itch by removing the promoter from the coding region of the Itch gene. Perry et al. (1998) concluded that the a18H mutation provides a link between ubiquitin-dependent proteolysis and normal immune function in vivo in addition to identifying a molecule important for the regulation of epithelial and hematopoietic cell growth. D'Andrea and Serhan (1998) presented models of how the disruption of the Itch locus may cause the immune reaction seen in a18H mice and discussed the implications for possible functions of Itch

[13131] It is appreciated that the abovementioned animal model

for ITCH is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13132] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13133] Perry, W. L.; Hustad, C. M.; Swing, D. A.; O'Sullivan, T. N.; Jenkins, N. A.; Copeland, N. G. : The itchy locus encodes a novel ubiquitin protein ligase that is disrupted in a18H mice. *Nature Genet.* 18: 143–146, 1998. ; and

[13134] Chen, X.; Wen, S.; Fukuda, M. N.; Gavva, N. R.; Hsu, D.; Akama, T. O.; Yang–Feng, T.; Shen, C. K. J. : Human ITCH is a coregulator of the hematopoietic transcription factor NF–E2. *Genomi.*

[13135] Further studies establishing the function and utilities of ITCH are found in John Hopkins OMIM database record ID 606409, and in cited publications numbered 4528–453 and 2569 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Integrin, Alpha 11 (ITGA11, Accession NM_012211) is another VGAM206 host target gene. ITGA11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ITGA11, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGA11 BINDING SITE, designated SEQ ID:14514, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13136] Another function of VGAM206 is therefore inhibition of Integrin, Alpha 11 (ITGA11, Accession NM_012211), a gene which acts as a collagen I receptor. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGA11. The function of ITGA11 has been established by previous studies. By screening a uterus cDNA library with an integrin-like cDNA fragment isolated from a fetal myoblast cDNA library, Velling et al. (1999) obtained a full-length cDNA sequence encoding integrin alpha-11. ITGA11 encodes a deduced 1,188-amino acid protein, including a 22-amino acid signal peptide. The mature 1,166-amino acid protein contains a 23-amino acid transmembrane region and a 24-amino acid cytoplasmic tail. It differs from most other integrin alpha chains in that the cytoplasmic tail contains the sequence GFFRS instead of the conserved GFFKR sequence. The extracellular do-

main contains 7 FG–GAP repeats with an I domain of 195 amino acids between repeats 2 and 3 that includes a conserved metal ion–dependent adhesion site motif. Twenty cysteines are located in the extracellular domain and there are 16 potential N–glycosylation sites. ITGA11 is 42%, 37%, and 35% identical with I domain alpha–integrins ITGA10 (OMIM Ref. No. 604042), ITGA1 (OMIM Ref. No. 192968), and ITGA2 (OMIM Ref. No. 192974), respectively. Northern blot analysis revealed expression of an approximately 5.5–kb ITGA11 transcript. Expression was highest in uterus, strong in heart, intermediate in skeletal muscle, stomach, small intestine, bladder, prostate, and colon, and low in nonmuscle tissues such as pancreas, kidney, and placenta. The authors found that, in contrast, ITGA1 is not expressed in the uterus. Immunoprecipitation studies and SDS–PAGE analysis showed that ITGA11 encodes a 145–kD protein, intermediate in size between ITGA2 or ITGA10 and ITGA1; the authors suggested that the difference is probably due to differential glycosylation. Like other I domain–containing integrins, ITGA11 binds to collagen. By sequence analysis, Lehnert et al. (1999) found that the deduced ITGA11 protein contains an I domain of 207 amino acids and 15 N–glycosylation sites in a mature

protein of 1167 amino acids. By FISH, Velling et al. (1999) mapped the ITGA11 gene to chromosome 15q23. By somatic cell hybrid analysis and FISH, Lehnert et al. (1999) mapped the gene to 15q22.3–q23.

[13137] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13138] Lehnert, K.; Ni, J.; Leung, E.; Gough, S. M.; Weaver, A.; Yao, W.-P.; Liu, D.; Wang, S.-X.; Morris, C. M.; Krissansen, G. W. : Cloning, sequence analysis, and chromosomal localization of the novel human integrin alpha-11 subunit (ITGA11). *Genomics* 60: 179–187, 1999. ; and

[13139] Velling, T.; Kusche-Gullberg, M.; Sejersen, T.; Gullberg, D. : cDNA cloning and chromosomal localization of human alpha-11 integrin: a collagen-binding, I domain-containing, beta-1-asso.

[13140] Further studies establishing the function and utilities of ITGA11 are found in John Hopkins OMIM database record ID 604789, and in cited publications numbered 2906–2907 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIP2 (Accession NM_006383) is another VGAM206 host target gene. KIP2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by KIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIP2 BINDING SITE, designated SEQ ID:13089, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13141] Another function of VGAM206 is therefore inhibition of KIP2 (Accession NM_006383). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIP2. Keratin 16 (focal non-epidermolytic palmoplantar keratoderma) (KRT16, Accession XM_170845) is another VGAM206 host target gene. KRT16 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KRT16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KRT16 BINDING SITE, designated SEQ ID:45630, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13142] Another function of VGAM206 is therefore inhibition of

Keratin 16 (focal non-epidermolytic palmoplantar keratoderma) (KRT16, Accession XM_170845). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KRT16. Leucine Zipper, Down-regulated In Cancer 1 (LDOC1, Accession NM_012317) is another VGAM206 host target gene. LDOC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LDOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDOC1 BINDING SITE, designated SEQ ID:14693, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13143] Another function of VGAM206 is therefore inhibition of Leucine Zipper, Down-regulated In Cancer 1 (LDOC1, Accession NM_012317). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDOC1. Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767) is another VGAM206 host target gene. LZTR1 BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by LZTR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTR1 BINDING SITE, designated SEQ ID:13640, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13144] Another function of VGAM206 is therefore inhibition of Leucine-zipper-like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTR1. Nyctalopin (NYX, Accession NM_022567) is another VGAM206 host target gene. NYX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NYX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYX BINDING SITE, designated SEQ ID:22889, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13145] Another function of VGAM206 is therefore inhibition of

Nyctalopin (NYX, Accession NM_022567), a gene which functions as the von willebrand factor receptor and mediates von willebrand factor-dependent platelet adhesion to blood vessels. the adhesion of platelets to injured vascular surfaces in the arterial circulation is a critical initiating event in hemostasis (by similarity). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYX. The function of NYX has been established by previous studies. By positional cloning and the candidate gene approach, directed at the elucidation of the defect in complete congenital stationary night blindness (CSNB1; 310500), Bech-Hansen et al. (2000) identified a novel gene, NYX, that encodes a protein (nyctalopin) of 481 amino acids. Nyctalopin shows sequence similarity with members of the superfamily of proteins containing tandem arrays of the leucine-rich repeat (LRR) motif, as well as other features qualifying the protein as a member of the subfamily of small leucine-rich proteoglycans (SLRPs). By PCR amplification of tissue-specific cDNA, Bech-Hansen et al. (2000) detected expression of NYX in retina and kidney only. In the retina it appeared to be expressed in photoreceptors, bipolar and amacrine interneurons, and ganglion cells.

Pusch et al. (2000) likewise detected 14 different mutations. In 3 families the gene was partially deleted. They found expression of the gene at low levels in retina, brain, testis, and muscle.

[13146] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13147] Bech-Hansen, N. T.; Naylor, M. J.; Maybaum, T. A.; Sparkes, R. L.; Koop, B.; Birch, D. G.; Bergen, A. A. B.; Prinsen, C. F. M.; Polomeno, R. C.; Gal, A.; Drack, A. V.; Musarella, M. A.; Jacobson, S. G.; Young, R. S. L.; Weleber, R. G. : Mutations in NYX, encoding the leucine-rich proteoglycan nyctalopin, cause X-linked complete congenital stationary night blindness. *Nature Genet.* 26: 319-323, 2000. ; and

[13148] Pusch, C. M.; Zeitze, C.; Brandau, O.; Pesch, K.; Achatz, H.; Feil, S.; Scharfe, C.; Maurer, J.; Jacobi, F. K.; Pinckers, A.; Andreasson, S.; Hardcastle, A.; Wissinger, B.; Berger, W.;

[13149] Further studies establishing the function and utilities of NYX are found in John Hopkins OMIM database record ID 300278, and in cited publications numbered 10994-10995 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130835) is another VGAM206 host target gene. OPA1 BINDING SITE1 through OPA1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OPA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA1 BINDING SITE1 through OPA1 BINDING SITE5, designated SEQ ID:28340, SEQ ID:28324, SEQ ID:28356, SEQ ID:28348 and SEQ ID:28332 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13150] Another function of VGAM206 is therefore inhibition of Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130835). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA1. PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_012231) is another VGAM206 host target gene. PRDM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM2, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM2 BINDING SITE, designated SEQ ID:14537, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13151] Another function of VGAM206 is therefore inhibition of PR Domain Containing 2, with ZNF Domain (PRDM2, Accession NM_012231), a gene which plays a role in transcriptional regulation during neuronal differentiation and pathogenesis of retinoblastoma. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM2. The function of PRDM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. Prostaglandin E Synthase (PTGES, Accession NM_004878) is another VGAM206 host target gene. PTGES BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGES BINDING SITE, designated SEQ ID:11312, to the

nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13152] Another function of VGAM206 is therefore inhibition of Prostaglandin E Synthase (PTGES, Accession NM_004878). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGES. Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961) is another VGAM206 host target gene. PTGIS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGIS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGIS BINDING SITE, designated SEQ ID:6668, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13153] Another function of VGAM206 is therefore inhibition of Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961), a gene which catalyzes the isomerization of prostaglandin h₂ to prostacyclin (= prostaglandin i₂). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions as-

sociated with PTGIS. The function of PTGIS has been established by previous studies. Yokoyama et al. (1996) demonstrated that the prostacyclin synthase gene, which they symbolized PTGIS, consists of 10 exons spanning approximately 60 kb. All the splice donor and acceptor sites conformed to the GT/AG rule. The major product of the primer extension analysis suggested that the transcription of the gene started from the positions around 49 bp upstream of the translation initiation codon. By fluorescence in situ hybridization, they demonstrated that the gene is located at 20q13.11–q13.13. Prostacyclin (also known as prostaglandin I₂) is a potent vasodilator and inhibitor of platelet aggregation. The enzyme prostacyclin synthase (EC 5.3.99.4) catalyzes the isomerization of prostaglandin H₂ (PGH₂) to prostacyclin. Wang and Chen (1996) noted that although it has absorbance spectral features characteristic of the cytochrome P450s, PGIS has no monooxygenase activity and does not require an external source of electrons to initiate its enzyme reaction. Prostacyclin synthase is the single member of family 8 of the cytochrome P450 superfamily (Nelson et al., 1996).

[13154] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [13155] Wang, L.-H.; Chen, L. : Organization of the gene encoding human prostacyclin synthase. *Biochem. Biophys. Res. Commun.* 226: 631–637, 1996. ; and
- [13156] Yokoyama, C.; Yabuki, T.; Inoue, H.; Tone, Y.; Hara, S.; Hatae, T.; Nagata, M.; Takahashi, E.-I.; Tanabe, T. : Human gene encoding prostacyclin synthase (PTGIS): genomic organization, ch.
- [13157] Further studies establishing the function and utilities of PTGIS are found in John Hopkins OMIM database record ID 601699, and in cited publications numbered 670 and 2859–2861 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Peroxisomal Membrane Protein 3, 35kDa (Zellweger syndrome) (PXMP3, Accession NM_000318) is another VGAM206 host target gene. PXMP3 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PXMP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXMP3 BINDING SITE, designated SEQ ID:5860, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2917.

[13158] Another function of VGAM206 is therefore inhibition of Peroxisomal Membrane Protein 3, 35kDa (Zellweger syndrome) (PXMP3, Accession NM_000318). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXMP3. RIG (Accession NM_006394) is another VGAM206 host target gene. RIG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RIG BINDING SITE, designated SEQ ID:13105, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13159] Another function of VGAM206 is therefore inhibition of RIG (Accession NM_006394), a gene which is ribosomal protein S15. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RIG. The function of RIG has been established by previous studies. The gene called Rig (rat insulinoma gene) was first isolated from a cDNA li-

brary of rat insulinomas. Its cognate gene has been found to be activated in various human tumors such as insulinomas, esophageal cancers, and colon cancers. Inoue et al. (1987) isolated a human insulinoma cDNA encoding the human homolog of RIG. Structural analysis indicated that the predicted 145-amino acid RIG protein may be a DNA-binding protein. Shiga et al. (1990) isolated the genomic sequence of human RIG from a genomic DNA library constructed from a human esophageal carcinoma and determined its complete nucleotide sequence. The gene is composed of about 3,000 nucleotides and divided into 4 exons separated by 3 introns. The transcription initiation site was located -46 bp upstream from the first ATG codon. Because of CpG islands in the 5-prime region and regions with a high GC content and because of the wide expression of RIG in tissues and cells, Shiga et al. (1990) suggested that RIG may belong to the class of 'housekeeping' genes, whose products are necessary for the growth of all cell types. The human genome contains at least 6 copies of RIG pseudogenes, 4 of which have the characteristics of processed pseudogenes. Kitagawa et al. (1991) demonstrated the normal function of RIG. They showed that the immunoreactivity to a monoclonal antibody

against the deduced Rig protein and the translation product of Rig mRNA comigrated with ribosomal protein S15. The amino acid sequence of ribosomal protein S15 purified from rat liver coincided with that deduced from the nucleotide sequence of Rig mRNA, but there were indications that the initiator methionine was removed and the succeeding alanyl residue was monoacetylated. The authors concluded that the product of the Rig gene is ribosomal protein S15. Animal model experiments lend further support to the function of RIG. By somatic cell hybrid and radiation hybrid mapping analyses, Kenmochi et al. (1998) mapped the human RPS15 gene to 19p.

[13160] It is appreciated that the abovementioned animal model for RIG is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13161] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13162] Kitagawa, M.; Takasawa, S.; Kikuchi, N.; Itoh, T.; Teraoka, H.; Yamamoto, H.; Okamoto, H. : Rig encodes ribosomal protein S15: the primary structure of mammalian ribosomal protein S15. FEBS Lett. 283: 210–214, 1991. ; and

- [13163] Kenmochi, N.; Kawaguchi, T.; Rozen, S.; Davis, E.; Goodman, N.; Hudson, T. J.; Tanaka, T.; Page, D. C. : A map of 75 human ribosomal protein genes. *Genome Res.* 8: 509–523, 1998.
- [13164] Further studies establishing the function and utilities of RIG are found in John Hopkins OMIM database record ID 180535, and in cited publications numbered 1239 and 12396–12397 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RNA (guanine–7–) Methyltransferase (RNMT, Accession NM_003799) is another VGAM206 host target gene. RNMT BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RNMT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNMT BINDING SITE, designated SEQ ID:9891, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.
- [13165] Another function of VGAM206 is therefore inhibition of RNA (guanine–7–) Methyltransferase (RNMT, Accession NM_003799), a gene which catalyzes the methylation of GpppN– at the guanine N7 position. Accordingly, utilities

of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNMT. The function of RNMT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178.SHC (Src homology 2 domain containing) Transforming Protein 1 (SHC1, Accession NM_003029) is another VGAM206 host target gene. SHC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SHC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHC1 BINDING SITE, designated SEQ ID:8972, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13166] Another function of VGAM206 is therefore inhibition of SHC (Src homology 2 domain containing) Transforming Protein 1 (SHC1, Accession NM_003029), a gene which couples activated growth factor receptors to a signaling pathway. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHC1. The function of SHC1

and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53. Solute Carrier Family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), Member 1 (SLC1A1, Accession NM_004170) is another VGAM206 host target gene. SLC1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A1 BINDING SITE, designated SEQ ID:10380, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13167] Another function of VGAM206 is therefore inhibition of Solute Carrier Family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), Member 1 (SLC1A1, Accession NM_004170), a gene which is a glutamate transporter, essential for terminating the postsynaptic action of glutamate by rapidly removing it from the synaptic cleft. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical condi-

tions associated with SLC1A1. The function of SLC1A1 has been established by previous studies. High-affinity glutamate transporters play an essential role in transporting glutamate across plasma membranes. In brain, these transporters are crucial in terminating the action of the excitatory neurotransmitter glutamate and in maintaining extracellular glutamate concentrations below neurotoxic levels. Functional defects of high-affinity glutamate transporters have been suggested to be involved in the pathophysiology of amyotrophic lateral sclerosis (OMIM Ref. No. 105400). In small intestine and kidney, in which the high-affinity glutamate transporter mediates net absorption of glutamate and aspartate across epithelial cells, an inborn error of glutamate transport is thought to cause dicarboxylicaminoaciduria (OMIM Ref. No. 222730). Kanai and Hediger (1992) isolated a cDNA encoding a high-affinity glutamate transporter, designated EAAC1, that also transports aspartate but not other amino acids. EAAC1 was found to be uniquely expressed throughout the body, particularly in brain (neurons), intestine, and kidney. By Southern analysis of a panel of human/rodent somatic cell hybrids and by fluorescence in situ hybridization (FISH), Smith et al. (1994) mapped the EAAC1 gene to 9p24. They

suggested that mutations in this gene may be responsible for dicarboxylicaminoaciduria or for a form of familial ALS separate from the form due to mutation in the SOD1 gene (OMIM Ref. No. 147450) on chromosome 21. Lin et al. (2001) used a yeast 2-hybrid assay to identify a protein that interacts with EAAC1. This protein, termed GTRAP3-18 (OMIM Ref. No. 605709), is expressed in numerous tissues, localizes to the cell membrane and cytoplasm, and specifically interacts with the carboxy-terminal intracellular domain of EAAC1. Increasing the expression of GTRAP3-18 in cells reduces EAAC1-mediated glutamate transport by lowering substrate affinity. The expression of GTRAP3-18 can be upregulated by retinoic acid, which results in a specific reduction of EAAC1-mediated glutamate transport. Lin et al. (2001) concluded that glutamate transport proteins can be regulated potently and that GTRAP can modulate the transport functions ascribed to EAAC1. GTRAP3-18 may be important in regulating the metabolic functions of EAAC1.

[13168] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13169] Kanai, Y.; Hediger, M. A. : Primary structure and functional

characterization of a high-affinity glutamate transporter.

Nature 360: 467-471, 1992. ; and

[13170] Smith, C. P.; Weremowicz, S.; Kanai, Y.; Stelzner, M.; Morton, C. C.; Hediger, M. A. : Assignment of the gene coding for the human high-affinity glutamate transporter EAAC1 to 9p24: pot.

[13171] Further studies establishing the function and utilities of SLC1A1 are found in John Hopkins OMIM database record ID 133550, and in cited publications numbered 3585-3587 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 2 (facilitated glucose/fructose transporter), Member 5 (SLC2A5, Accession NM_003039) is another VGAM206 host target gene. SLC2A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A5 BINDING SITE, designated SEQ ID:9001, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13172] Another function of VGAM206 is therefore inhibition of

Solute Carrier Family 2 (facilitated glucose/fructose transporter), Member 5 (SLC2A5, Accession NM_003039), a gene which has probable role as a fructose transporter. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A5. The function of SLC2A5 has been established by previous studies. Davidson et al. (1992) showed that the glucose transporter isoform, GLUT5, is expressed on the brush border membrane of human small intestinal enterocytes. Burant et al. (1992) showed further that GLUT5 is a fructose transporter and may be largely responsible for the uptake of fructose from the lumen of the small intestine. GLUT2, which is present on the basolateral membrane of enterocytes, probably mediates the efflux of fructose from these cells. In addition, GLUT5 is probably responsible for the uptake of fructose by spermatozoa. The pattern of GLUT5 immunoreactivity in maturing spermatids suggested that the expression of GLUT5 may serve as a marker for terminal maturation of male germ cells. An increasing fraction of calories consumed in Western diets is derived from fructose. Increases in fructose consumption have been implicated in a rising incidence of hypertriglyceridemia and hyperinsulinemia. Mu-

tations in the small intestinal sodium/glucose cotransporter (OMIM Ref. No. 182380), which effectively abolish glucose uptake, have no effect on the absorption of fructose, indicating a separate fructose carrier protein. Using cDNA probes for Southern blotting of DNA from somatic cell hybrids and for in situ hybridization, Fan et al. (1989) showed that the GLUT5 gene (also symbolized SLC2A5) is located on chromosome 1. Also see Kayano et al. (1990). White et al. (1998) concluded that the correct assignment of SLC2A5 is 1p36.2. This was confirmed by use of somatic cell and radiation hybrid mapping panels and was consistent with previous EST mapping data. The carbonic anhydrase-6 (CA6; 114780) and alpha-enolase (ENO1; 172430) genes were physically linked to SLC2A5 in yeast- and P1-artificial chromosome (YAC and PAC) contigs. PACs from the contig were mapped to 1p36.2 by fluorescence in situ hybridization.

[13173] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13174] Davidson, N. O.; Hausman, A. M. L.; Ifkovits, C. A.; Buse, J. B.; Gould, G. W.; Burant, C. F.; Bell, G. I. : Human intestinal glucose transporter expression and localization of GLUT5.

Am. J. Physiol. 262: C795–C800, 1992. ; and

[13175] White, P. S.; Jensen, S. J.; Rajalingam, V.; Stairs, D.; Sulman, E. P.; Maris, J. M.; Biegel, J. A.; Wooster, R.; Brodeur, G. M. : Physical mapping of the CA6, ENO1, and SLC2A5 (GLUT5) gene.

[13176] Further studies establishing the function and utilities of SLC2A5 are found in John Hopkins OMIM database record ID 138230, and in cited publications numbered 12195–12196, 1190 and 11911 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na⁺/H⁺, amiloride sensitive) (SLC9A1, Accession XM_046881) is another VGAM206 host target gene. SLC9A1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC9A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A1 BINDING SITE, designated SEQ ID:34856, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13177] Another function of VGAM206 is therefore inhibition of

Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 1 (antiporter, Na^+/H^+ , amiloride sensitive) (SLC9A1, Accession XM_046881), a gene which is involved in pH regulation to eliminate acids generated by active metabolism or to counter adverse environmental conditions. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A1. The function of SLC9A1 has been established by previous studies. Denker et al. (2000) showed that the plasma membrane ion exchanger NHE1 acts as an anchor for actin filaments to control the integrity of the cortical cytoskeleton. This occurs through a previously unrecognized structural link between NHE1 and the actin-binding proteins ezrin (OMIM Ref. No. 123900), radixin (OMIM Ref. No. 179410), and moesin (OMIM Ref. No. 309845), which are collectively referred to as ERM proteins. NHE1 and ERM proteins were found to associate directly and colocalize in lamellipodia. Fibroblasts expressing NHE1 with mutations that disrupted binding with ERM proteins but not ion translocation had impaired organization of focal adhesions and actin stress fibers and an irregular cell shape. Denker et al. (2000) proposed a structural role for NHE1 in regulating the cortical cy-

toskeleton that is independent of its function as an ion exchanger. The genomic probe reported by Mattei et al. (1987) was used to map the APNH gene to 1p36.1–p35 by in situ hybridization (Mattei et al., 1988). Mattei et al. (1989) used in situ hybridization of the human cDNA probe to map the antiporter gene to the distal portion of mouse chromosome 4 and to the long arm of Chinese hamster chromosome 2, confirming the conserved homology between the distal part of human chromosome 1p, the mouse distal 4, and Chinese hamster distal 2q. By the analysis of fragment length variations in recombinant inbred strains, Morahan and Rakar (1993) likewise mapped the Nhe1 gene to mouse chromosome 4, between Lck and Akp2. Lifton et al. (1990) used genomic clones of the SLC9A1 gene to identify 2 polymorphisms. Using these RFLPs in 59 reference families, they found that the antiporter gene lies 3 cM proximal to the RH locus. Dudley et al. (1990) PCR-amplified a 376-bp fragment corresponding to the 5-prime end of SLC9A1 and detected a polymorphism within this fragment by denaturing gradient gel electrophoresis. By genetic linkage studies, they mapped SLC9A1 telomeric to D1S57 and close to RH (OMIM Ref. No. 111700) and ALPL (OMIM Ref. No.

171760). They pointed out that SLC9A1 is a plausible candidate gene for human essential hypertension.

[13178] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13179] Denker, S. P.; Huang, D. C.; Orlowski, J.; Furthmayr, H.; Barber, D. L. : Direct binding of the Na-H exchanger NHE1 to ERM proteins regulates the cortical cytoskeleton and cell shape independently of H(+) translocation. Molec. Cell 6: 1425-1436, 2000. ; and

[13180] Dudley, C. R. K.; Giuffra, L. A.; Tippet, P.; Kidd, K. K.; Reenders, S. T. : The Na⁺/H⁺ antiporter: a 'melt' polymorphism allows regional mapping to the short arm of chromosome 1. Hum. G.

[13181] Further studies establishing the function and utilities of SLC9A1 are found in John Hopkins OMIM database record ID 107310, and in cited publications numbered 4068-4077 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily C, Member 1 (SMARCC1, Accession NM_003074) is another VGAM206 host target gene. SMARCC1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by SMARCC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCC1 BINDING SITE, designated SEQ ID:9042, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13182] Another function of VGAM206 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily C, Member 1 (SMARCC1, Accession NM_003074), a gene which is involved in chromatin remodeling. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCC1. The function of SMARCC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM57. Steroidogenic Acute Regulatory Protein (STAR, Accession NM_000349) is another VGAM206 host target gene. STAR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAR, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAR BINDING SITE, designated SEQ ID:5905, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13183] Another function of VGAM206 is therefore inhibition of Steroidogenic Acute Regulatory Protein (STAR, Accession NM_000349). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAR. Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544) is another VGAM206 host target gene. TAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TAP2 BINDING SITE, designated SEQ ID:6143, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13184] Another function of VGAM206 is therefore inhibition of Transporter 2, ATP-binding Cassette, Sub-family B (MDR/TAP) (TAP2, Accession NM_000544), a gene which is

involved in the transport of antigens from the cytoplasm to a membrane-bound compartment for association with mhc class i molecules. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TAP2. The function of TAP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257) is another VGAM206 host target gene. TJP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TJP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TJP1 BINDING SITE, designated SEQ ID:9267, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13185] Another function of VGAM206 is therefore inhibition of Tight Junction Protein 1 (zona occludens 1) (TJP1, Accession NM_003257), a gene which colocalizes and interacts with cadherins in cells lacking tight junctions. Accordingly, utilities of VGAM206 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with TJP1. The function of TJP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Ubiquitin-like 1 (sentrin) (UBL1, Accession NM_003352) is another VGAM206 host target gene. UBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBL1 BINDING SITE, designated SEQ ID:9380, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13186] Another function of VGAM206 is therefore inhibition of Ubiquitin-like 1 (sentrin) (UBL1, Accession NM_003352), a gene which generates proteins resistant to degradation through its modification. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBL1. The function of UBL1 has been established by previous studies. Activation of NF-kappa-B is achieved by ubiquitination and proteasome-mediated degradation of I-

kappa-B-alpha (OMIM Ref. No. 164008). Desterro et al. (1998) detected modified I-kappa-B-alpha, conjugated to the small ubiquitin-like protein SUMO1, which is resistant to signal-induced degradation. Overexpression of SUMO1 inhibits signal-induced activation of NF-kappa-B-dependent transcription. SUMO1 modification of I-kappa-B-alpha is inhibited by phosphorylation. Thus, while ubiquitination targets proteins for rapid degradation, SUMO1 modification acts antagonistically to generate proteins resistant to degradation. Many antibiotics, anti-cancer drugs, toxins, carcinogens, and physiologic stresses abort the catalytic cycles of topoisomerases (see OMIM Ref. No. TOP1, 126420), resulting in topoisomerase-mediated DNA damage. Mao et al. (2000) showed that camptothecin, a TOP1-specific poison, can induce rapid and extensive conjugation of SUMO1 to human DNA. This and other observations suggested that SUMO1 may be involved in the repair of TOP1-mediated DNA damage.

[13187] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13188] Desterro, J. M. P.; Rodriguez, M. S.; Hay, R. T. : SUMO-1 modification of I-kappa-B-alpha inhibits NF-kappa-B ac-

tivation. Molec. Cell 2: 233–239, 1998. ; and

[13189] Mao, Y.; Sun, M.; Desai, S. D.; Liu, L. F. : SUMO–1 conjugation to topoisomerase I: a possible repair response to topoisomerase–mediated DNA damage. Proc. Nat. Acad. Sci. 97: 4046–4051.

[13190] Further studies establishing the function and utilities of UBL1 are found in John Hopkins OMIM database record ID 601912, and in cited publications numbered 9134–9139 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Uracil–DNA Glycosylase (UNG, Accession NM_003362) is another VGAM206 host target gene. UNG BINDING SITE1 and UNG BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by UNG, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNG BINDING SITE1 and UNG BINDING SITE2, designated SEQ ID:9390 and SEQ ID:28128 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13191] Another function of VGAM206 is therefore inhibition of Uracil–DNA Glycosylase (UNG, Accession NM_003362), a

gene which excises uracil residues from the dna to prevent mutagenesis and initiate the base-excision repair (BER) pathway. Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNG. The function of UNG has been established by previous studies. Uracil DNA glycosylase removes uracil in DNA resulting from deamination of cytosine or replicative incorporation of dUMP instead of dTMP (Haug et al., 1996). Animal model experiments lend further support to the function of UNG. Nilsen et al. (2000) generated knockout mice lacking Ung. In contrast to Ung – mutants of bacteria and yeast, these mice did not exhibit a greatly increased spontaneous mutation frequency. There was, however, only slow removal of uracil from misincorporated dUMP in isolated Ung –/– nuclei and an elevated steady-state level of uracil in DNA in dividing Ung –/– cells. A backup uracil-excising activity in tissue extracts from Ung null mice, with properties indistinguishable from the mammalian SMUG1 DNA glycosylase, may account for the repair of premutagenic U:G mispairs resulting from cytosine deamination in vivo. The authors suggested that the nuclear UNG protein has evolved a specialized role in mammalian cells counteract–

ing U:A base pairs formed by use of dUTP during DNA synthesis.

[13192] It is appreciated that the abovementioned animal model for UNG is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13193] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13194] Haug, T.; Skorpen, F.; Kvaloy, K.; Eftedal, I.; Lund, H.; Krokan, H. E. : Human uracil–DNA glycosylase gene: sequence organization, methylation pattern, and mapping to chromosome 12q23–q24.1. *Genomics* 36: 408–416, 1996. ; and

[13195] Nilsen, H.; Rosewell, I.; Robins, P.; Skjelbred, C. F.; Andersen, S.; Slupphaug, G.; Daly, G.; Krokan, H. E.; Lindahl, T.; Barnes, D. E. : Uracil–DNA glycosylase (UNG)–deficient mice rev.

[13196] Further studies establishing the function and utilities of UNG are found in John Hopkins OMIM database record ID 191525, and in cited publications numbered 12619–12626 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc

Finger Protein 74 (Cos52) (ZNF74, Accession NM_003426) is another VGAM206 host target gene. ZNF74 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ZNF74, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF74 BINDING SITE, designated SEQ ID:9471, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13197] Another function of VGAM206 is therefore inhibition of Zinc Finger Protein 74 (Cos52) (ZNF74, Accession NM_003426). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF74. ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726) is another VGAM206 host target gene. ABCC13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ABCC13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCC13 BINDING SITE, designated SEQ

ID:28974, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13198] Another function of VGAM206 is therefore inhibition of ATP-binding Cassette, Sub-family C (CFTR/MRP), Member 13 (ABCC13, Accession NM_138726). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCC13. Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM_015049) is another VGAM206 host target gene. ALS2CR3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ALS2CR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALS2CR3 BINDING SITE, designated SEQ ID:17414, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13199] Another function of VGAM206 is therefore inhibition of Amyotrophic Lateral Sclerosis 2 (juvenile) Chromosome Region, Candidate 3 (ALS2CR3, Accession NM_015049).

Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALS2CR3. AP1 Gamma Subunit Binding Protein 1 (AP1GBP1, Accession NM_080551) is another VGAM206 host target gene. AP1GBP1 BINDING SITE1 through AP1GBP1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AP1GBP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1GBP1 BINDING SITE1 through AP1GBP1 BINDING SITE5, designated SEQ ID:27882, SEQ ID:27874, SEQ ID:14118, SEQ ID:27873 and SEQ ID:14119 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13200] Another function of VGAM206 is therefore inhibition of AP1 Gamma Subunit Binding Protein 1 (AP1GBP1, Accession NM_080551). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1GBP1. Chromosome 20 Open Reading Frame 164 (C20orf164, Accession XM_086633) is another VGAM206 host target gene.

C20orf164 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf164 BINDING SITE, designated SEQ ID:38802, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13201] Another function of VGAM206 is therefore inhibition of Chromosome 20 Open Reading Frame 164 (C20orf164, Accession XM_086633). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf164. Chromosome 20 Open Reading Frame 177 (C20orf177, Accession XM_030726) is another VGAM206 host target gene. C20orf177 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf177, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf177 BINDING SITE, designated SEQ ID:31129, to the nucleotide sequence of VGAM206 RNA,

herein designated VGAM RNA, also designated SEQ ID:2917.

[13202] Another function of VGAM206 is therefore inhibition of Chromosome 20 Open Reading Frame 177 (C20orf177, Accession XM_030726). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf177. COAS3 (Accession NM_139020) is another VGAM206 host target gene. COAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COAS3 BINDING SITE, designated SEQ ID:29123, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13203] Another function of VGAM206 is therefore inhibition of COAS3 (Accession NM_139020). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COAS3. COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM_022730) is an–

other VGAM206 host target gene. COPS7B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COPS7B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COPS7B BINDING SITE, designated SEQ ID:22932, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13204] Another function of VGAM206 is therefore inhibition of COP9 Constitutive Photomorphogenic Homolog Subunit 7B (Arabidopsis) (COPS7B, Accession NM_022730). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COPS7B. CSL4 (Accession NM_016046) is another VGAM206 host target gene. CSL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSL4 BINDING SITE, designated SEQ ID:18126, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA,

also designated SEQ ID:2917.

[13205] Another function of VGAM206 is therefore inhibition of CSL4 (Accession NM_016046). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSL4. Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734) is another VGAM206 host target gene. DCAMKL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCAMKL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCAMKL1 BINDING SITE, designated SEQ ID:11113, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13206] Another function of VGAM206 is therefore inhibition of Doublecortin and CaM Kinase-like 1 (DCAMKL1, Accession NM_004734). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCAMKL1. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681) is another VGAM206 host target

gene. DDX34 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DDX34, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX34 BINDING SITE, designated SEQ ID:16159, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13207] Another function of VGAM206 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 34 (DDX34, Accession NM_014681). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX34. DKFZp434C0328 (Accession NM_017577) is another VGAM206 host target gene. DKFZp434C0328 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZp434C0328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0328 BINDING SITE, designated SEQ ID:19016, to the nucleotide sequence of VGAM206

RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13208] Another function of VGAM206 is therefore inhibition of DKFZp434C0328 (Accession NM_017577). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0328. DKFZP434H132 (Accession XM_057020) is another VGAM206 host target gene. DKFZP434H132 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434H132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H132 BINDING SITE, designated SEQ ID:36451, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13209] Another function of VGAM206 is therefore inhibition of DKFZP434H132 (Accession XM_057020). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H132. DKFZP434L1435 (Accession XM_175250) is another VGAM206 host target gene. DK-

FZP434L1435 BINDING SITE1 through DKFZP434L1435 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DKFZP434L1435, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L1435 BINDING SITE1 through DKFZP434L1435 BINDING SITE3, designated SEQ ID:46703, SEQ ID:44269 and SEQ ID:46665 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13210] Another function of VGAM206 is therefore inhibition of DKFZP434L1435 (Accession XM_175250). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L1435. DKFZP564I052 (Accession XM_039660) is another VGAM206 host target gene. DKFZP564I052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I052 BINDING SITE, des-

ignated SEQ ID:33137, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13211] Another function of VGAM206 is therefore inhibition of DKFZP564I052 (Accession XM_039660). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I052. DnaJ (Hsp40) Homolog, Subfamily A, Member 2 (DNAJA2, Accession XM_007963) is another VGAM206 host target gene. DNAJA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJA2 BINDING SITE, designated SEQ ID:30069, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13212] Another function of VGAM206 is therefore inhibition of DnaJ (Hsp40) Homolog, Subfamily A, Member 2 (DNAJA2, Accession XM_007963). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJA2. Docking

Protein 4 (DOK4, Accession NM_018110) is another VGAM206 host target gene. DOK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DOK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DOK4 BINDING SITE, designated SEQ ID:19881, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13213] Another function of VGAM206 is therefore inhibition of Docking Protein 4 (DOK4, Accession NM_018110). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOK4. Down Syndrome Critical Region Gene 1-like 1 (DSCR1L1, Accession NM_005822) is another VGAM206 host target gene. DSCR1L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DSCR1L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSCR1L1 BINDING SITE, designated SEQ ID:12432, to the nucleotide

sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13214] Another function of VGAM206 is therefore inhibition of Down Syndrome Critical Region Gene 1-like 1 (DSCR1L1, Accession NM_005822). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSCR1L1. Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969) is another VGAM206 host target gene. EIF5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EIF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF5 BINDING SITE, designated SEQ ID:7699, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13215] Another function of VGAM206 is therefore inhibition of Eukaryotic Translation Initiation Factor 5 (EIF5, Accession NM_001969). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF5. FLJ10477 (Accession NM_018105) is another VGAM206 host target gene.

FLJ10477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10477 BINDING SITE, designated SEQ ID:19875, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13216] Another function of VGAM206 is therefore inhibition of FLJ10477 (Accession NM_018105). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10477. FLJ10781 (Accession NM_018215) is another VGAM206 host target gene. FLJ10781 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10781, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10781 BINDING SITE, designated SEQ ID:20140, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13217] Another function of VGAM206 is therefore inhibition of FLJ10781 (Accession NM_018215). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10781. FLJ10898 (Accession XM_002486) is another VGAM206 host target gene. FLJ10898 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10898, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10898 BINDING SITE, designated SEQ ID:29895, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13218] Another function of VGAM206 is therefore inhibition of FLJ10898 (Accession XM_002486). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10898. FLJ12221 (Accession XM_031342) is another VGAM206 host target gene. FLJ12221 BINDING SITE1 and FLJ12221 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12221, corresponding to HOST TARGET binding sites such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12221 BINDING SITE1 and FLJ12221 BINDING SITE2, designated SEQ ID:31348 and SEQ ID:31347 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13219] Another function of VGAM206 is therefore inhibition of FLJ12221 (Accession XM_031342). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12221. FLJ12484 (Accession NM_022767) is another VGAM206 host target gene. FLJ12484 BINDING SITE1 through FLJ12484 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ12484, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12484 BINDING SITE1 through FLJ12484 BINDING SITE4, designated SEQ ID:23021, SEQ ID:34519, SEQ ID:23022 and SEQ ID:34520 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13220] Another function of VGAM206 is therefore inhibition of

FLJ12484 (Accession NM_022767). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12484. FLJ12707 (Accession NM_022067) is another VGAM206 host target gene. FLJ12707 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12707 BINDING SITE, designated SEQ ID:22609, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13221] Another function of VGAM206 is therefore inhibition of FLJ12707 (Accession NM_022067). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12707. FLJ13096 (Accession NM_025000) is another VGAM206 host target gene. FLJ13096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ13096 BINDING SITE, designated SEQ ID:24569, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13222] Another function of VGAM206 is therefore inhibition of FLJ13096 (Accession NM_025000). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13096. FLJ13984 (Accession NM_024770) is another VGAM206 host target gene. FLJ13984 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13984, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13984 BINDING SITE, designated SEQ ID:24131, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13223] Another function of VGAM206 is therefore inhibition of FLJ13984 (Accession NM_024770). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13984. FLJ14457 (Accession NM_032788) is another VGAM206

host target gene. FLJ14457 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ14457, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14457 BINDING SITE, designated SEQ ID:26543, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13224] Another function of VGAM206 is therefore inhibition of FLJ14457 (Accession NM_032788). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14457. FLJ20051 (Accession NM_019087) is another VGAM206 host target gene. FLJ20051 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20051 BINDING SITE, designated SEQ ID:21164, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13225] Another function of VGAM206 is therefore inhibition of FLJ20051 (Accession NM_019087). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20051. FLJ20508 (Accession NM_017850) is another VGAM206 host target gene. FLJ20508 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20508, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20508 BINDING SITE, designated SEQ ID:19521, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13226] Another function of VGAM206 is therefore inhibition of FLJ20508 (Accession NM_017850). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20508. FLJ20984 (Accession NM_024630) is another VGAM206 host target gene. FLJ20984 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20984, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20984 BINDING SITE, designated SEQ ID:23896, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13227] Another function of VGAM206 is therefore inhibition of FLJ20984 (Accession NM_024630). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20984. FLJ21302 (Accession NM_022901) is another VGAM206 host target gene. FLJ21302 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21302 BINDING SITE, designated SEQ ID:23187, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13228] Another function of VGAM206 is therefore inhibition of FLJ21302 (Accession NM_022901). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21302.

FLJ22283 (Accession NM_032220) is another VGAM206 host target gene. FLJ22283 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ22283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22283 BINDING SITE, designated SEQ ID:25948, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13229] Another function of VGAM206 is therefore inhibition of FLJ22283 (Accession NM_032220). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22283. FLJ31951 (Accession NM_144726) is another VGAM206 host target gene. FLJ31951 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ31951, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31951 BINDING SITE, designated SEQ ID:29553, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2917.

[13230] Another function of VGAM206 is therefore inhibition of FLJ31951 (Accession NM_144726). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31951. Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077) is another VGAM206 host target gene. GOLGA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GOLGA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GOLGA1 BINDING SITE, designated SEQ ID:7866, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13231] Another function of VGAM206 is therefore inhibition of Golgi Autoantigen, Golgin Subfamily A, 1 (GOLGA1, Accession NM_002077). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GOLGA1. HTGN29 (Accession NM_020199) is another VGAM206 host target gene. HTGN29 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by HTGN29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTGN29 BINDING SITE, designated SEQ ID:21434, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13232] Another function of VGAM206 is therefore inhibition of HTGN29 (Accession NM_020199). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTGN29. Interleukin 14 (IL14, Accession XM_170924) is another VGAM206 host target gene. IL14 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by IL14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL14 BINDING SITE, designated SEQ ID:45703, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13233] Another function of VGAM206 is therefore inhibition of

Interleukin 14 (IL14, Accession XM_170924). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL14. KBRAS2 (Accession NM_017595) is another VGAM206 host target gene. KBRAS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KBRAS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KBRAS2 BINDING SITE, designated SEQ ID:19048, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13234] Another function of VGAM206 is therefore inhibition of KBRAS2 (Accession NM_017595). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KBRAS2. Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186) is another VGAM206 host target gene. KCNB2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNB2 BINDING SITE, designated SEQ ID:45965, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13235] Another function of VGAM206 is therefore inhibition of Potassium Voltage-gated Channel, Shab-related Subfamily, Member 2 (KCNB2, Accession XM_171186). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNB2. KIAA0227 (Accession XM_027236) is another VGAM206 host target gene. KIAA0227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0227 BINDING SITE, designated SEQ ID:30457, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13236] Another function of VGAM206 is therefore inhibition of KIAA0227 (Accession XM_027236). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0227. KIAA0332 (Accession XM_031553) is another VGAM206 host target gene. KIAA0332 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0332 BINDING SITE, designated SEQ ID:31419, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13237] Another function of VGAM206 is therefore inhibition of KIAA0332 (Accession XM_031553). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0332. KIAA0416 (Accession NM_015564) is another VGAM206 host target gene. KIAA0416 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0416 BINDING SITE, designated SEQ ID:17839, to the

nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13238] Another function of VGAM206 is therefore inhibition of KIAA0416 (Accession NM_015564). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0416. KIAA0469 (Accession NM_014851) is another VGAM206 host target gene. KIAA0469 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0469, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0469 BINDING SITE, designated SEQ ID:16896, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13239] Another function of VGAM206 is therefore inhibition of KIAA0469 (Accession NM_014851). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0469. KIAA0620 (Accession XM_030707) is another VGAM206 host target gene. KIAA0620 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA0620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0620 BINDING SITE, designated SEQ ID:31121, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13240] Another function of VGAM206 is therefore inhibition of KIAA0620 (Accession XM_030707). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0620. KIAA0748 (Accession NM_014796) is another VGAM206 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16705, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13241] Another function of VGAM206 is therefore inhibition of KIAA0748 (Accession NM_014796). Accordingly, utilities

of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. KIAA0763 (Accession NM_014869) is another VGAM206 host target gene. KIAA0763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0763 BINDING SITE, designated SEQ ID:16971, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13242] Another function of VGAM206 is therefore inhibition of KIAA0763 (Accession NM_014869). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0763. KIAA0836 (Accession XM_035390) is another VGAM206 host target gene. KIAA0836 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0836, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0836 BINDING SITE, designated SEQ ID:32251, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13243] Another function of VGAM206 is therefore inhibition of KIAA0836 (Accession XM_035390). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0836. KIAA0930 (Accession XM_047214) is another VGAM206 host target gene. KIAA0930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0930 BINDING SITE, designated SEQ ID:34919, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13244] Another function of VGAM206 is therefore inhibition of KIAA0930 (Accession XM_047214). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0930. KIAA1026 (Accession XM_048825) is another VGAM206 host target gene. KIAA1026 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35279, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13245] Another function of VGAM206 is therefore inhibition of KIAA1026 (Accession XM_048825). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. KIAA1056 (Accession NM_014894) is another VGAM206 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17051, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13246] Another function of VGAM206 is therefore inhibition of

KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. KIAA1078 (Accession XM_036589) is another VGAM206 host target gene. KIAA1078 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1078, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1078 BINDING SITE, designated SEQ ID:32475, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13247] Another function of VGAM206 is therefore inhibition of KIAA1078 (Accession XM_036589). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1078. KIAA1171 (Accession XM_113868) is another VGAM206 host target gene. KIAA1171 BINDING SITE1 and KIAA1171 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA1171, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1171 BINDING SITE1 and KIAA1171 BINDING SITE2, designated SEQ ID:42484 and SEQ ID:42483 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13248] Another function of VGAM206 is therefore inhibition of KIAA1171 (Accession XM_113868). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1171. KIAA1297 (Accession XM_051005) is another VGAM206 host target gene. KIAA1297 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1297 BINDING SITE, designated SEQ ID:35719, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13249] Another function of VGAM206 is therefore inhibition of KIAA1297 (Accession XM_051005). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1297. KIAA1354 (Accession XM_027604) is another VGAM206 host target gene. KIAA1354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1354 BINDING SITE, designated SEQ ID:30542, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13250] Another function of VGAM206 is therefore inhibition of KIAA1354 (Accession XM_027604). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1354. KIAA1391 (Accession XM_040866) is another VGAM206 host target gene. KIAA1391 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1391 BINDING SITE, designated SEQ ID:33403, to the

nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13251] Another function of VGAM206 is therefore inhibition of KIAA1391 (Accession XM_040866). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1391. KIAA1571 (Accession XM_027744) is another VGAM206 host target gene. KIAA1571 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1571, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1571 BINDING SITE, designated SEQ ID:30568, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13252] Another function of VGAM206 is therefore inhibition of KIAA1571 (Accession XM_027744). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1571. KIAA1753 (Accession XM_036115) is another VGAM206 host target gene. KIAA1753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1753 BINDING SITE, designated SEQ ID:32382, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13253] Another function of VGAM206 is therefore inhibition of KIAA1753 (Accession XM_036115). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1753. KIAA1855 (Accession XM_166453) is another VGAM206 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44362, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13254] Another function of VGAM206 is therefore inhibition of KIAA1855 (Accession XM_166453). Accordingly, utilities

of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. KIAA1872 (Accession XM_031917) is another VGAM206 host target gene. KIAA1872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31523, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13255] Another function of VGAM206 is therefore inhibition of KIAA1872 (Accession XM_031917). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. I(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM_114201) is another VGAM206 host target gene. L3MBTL2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by L3MBTL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of L3MBTL2 BINDING SITE, designated SEQ ID:42794, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13256] Another function of VGAM206 is therefore inhibition of l(3)mbt-like 2 (Drosophila) (L3MBTL2, Accession XM_114201). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with L3MBTL2. LEC3 (Accession NM_015236) is another VGAM206 host target gene. LEC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEC3 BINDING SITE, designated SEQ ID:17573, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13257] Another function of VGAM206 is therefore inhibition of LEC3 (Accession NM_015236). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEC3. LIN-7-C (Accession NM_018362) is another VGAM206

host target gene. LIN-7-C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIN-7-C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIN-7-C BINDING SITE, designated SEQ ID:20370, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13258] Another function of VGAM206 is therefore inhibition of LIN-7-C (Accession NM_018362). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIN-7-C. Lipase, Member I (LIPI, Accession XM_086767) is another VGAM206 host target gene. LIPI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LIPI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIPI BINDING SITE, designated SEQ ID:38844, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13259] Another function of VGAM206 is therefore inhibition of Lipase, Member I (LIPI, Accession XM_086767). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIPI. MGC10715 (Accession NM_024325) is another VGAM206 host target gene. MGC10715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC10715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC10715 BINDING SITE, designated SEQ ID:23618, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13260] Another function of VGAM206 is therefore inhibition of MGC10715 (Accession NM_024325). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC10715. MGC20576 (Accession NM_144691) is another VGAM206 host target gene. MGC20576 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC20576, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20576 BINDING SITE, designated SEQ ID:29511, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13261] Another function of VGAM206 is therefore inhibition of MGC20576 (Accession NM_144691). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20576. MGC3123 (Accession NM_024107) is another VGAM206 host target gene. MGC3123 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC3123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3123 BINDING SITE, designated SEQ ID:23552, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13262] Another function of VGAM206 is therefore inhibition of MGC3123 (Accession NM_024107). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

MGC3123. MGC5302 (Accession NM_024089) is another VGAM206 host target gene. MGC5302 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC5302, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC5302 BINDING SITE, designated SEQ ID:23531, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13263] Another function of VGAM206 is therefore inhibition of MGC5302 (Accession NM_024089). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC5302. MGC9753 (Accession NM_033419) is another VGAM206 host target gene. MGC9753 BINDING SITE1 and MGC9753 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MGC9753, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC9753 BINDING SITE1 and MGC9753 BINDING SITE2, designated SEQ ID:27245 and SEQ ID:27239 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13264] Another function of VGAM206 is therefore inhibition of MGC9753 (Accession NM_033419). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC9753. MPPE1 (Accession NM_023075) is another VGAM206 host target gene. MPPE1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region

of mRNA encoded by MPPE1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPPE1 BINDING SITE, designated SEQ ID:23333, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13265] Another function of VGAM206 is therefore inhibition of MPPE1 (Accession NM_023075). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPPE1. p21(CDKN1A)-activated Kinase 7 (PAK7, Accession XM_045653) is another VGAM206 host target gene. PAK7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAK7 BINDING SITE, designated SEQ ID:34511, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13266] Another function of VGAM206 is therefore inhibition of p21(CDKN1A)-activated Kinase 7 (PAK7, Accession

XM_045653). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK7. Phospholipid Scramblase 3 (PLSCR3, Accession XM_165421) is another VGAM206 host target gene. PLSCR3 BINDING SITE1 and PLSCR3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PLSCR3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLSCR3 BINDING SITE1 and PLSCR3 BINDING SITE2, designated SEQ ID:43638 and SEQ ID:21633 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13267] Another function of VGAM206 is therefore inhibition of Phospholipid Scramblase 3 (PLSCR3, Accession XM_165421). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLSCR3. PRO1430 (Accession NM_018599) is another VGAM206 host target gene. PRO1430 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded

by PRO1430, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1430 BINDING SITE, designated SEQ ID:20676, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13268] Another function of VGAM206 is therefore inhibition of PRO1430 (Accession NM_018599). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1430. RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM_004283) is another VGAM206 host target gene. RAB3D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB3D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB3D BINDING SITE, designated SEQ ID:10494, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13269] Another function of VGAM206 is therefore inhibition of

RAB3D, Member RAS Oncogene Family (RAB3D, Accession NM_004283). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB3D. RABEX5 (Accession NM_014504) is another VGAM206 host target gene.

RABEX5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RABEX5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RABEX5 BINDING SITE, designated SEQ ID:15838, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13270] Another function of VGAM206 is therefore inhibition of RABEX5 (Accession NM_014504). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RABEX5. Regulator of G-protein Signalling 11 (RGS11, Accession NM_003834) is another VGAM206 host target gene. RGS11 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RGS11, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RGS11 BINDING SITE, designated SEQ ID:9926, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13271] Another function of VGAM206 is therefore inhibition of Regulator of G-protein Signalling 11 (RGS11, Accession NM_003834). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RGS11. RNAHP (Accession NM_007372) is another VGAM206 host target gene. RNAHP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNAHP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNAHP BINDING SITE, designated SEQ ID:14301, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13272] Another function of VGAM206 is therefore inhibition of RNAHP (Accession NM_007372). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with RNAHP. RoXaN (Accession NM_025013) is another VGAM206 host target gene. RoXaN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RoXaN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RoXaN BINDING SITE, designated SEQ ID:24606, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13273] Another function of VGAM206 is therefore inhibition of RoXaN (Accession NM_025013). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RoXaN. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942) is another VGAM206 host target gene. RPS6KA4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RPS6KA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA4 BINDING SITE,

designated SEQ ID:10057, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13274] Another function of VGAM206 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 4 (RPS6KA4, Accession NM_003942). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA4. Syndecan Binding Protein (syntenin) (SDCBP, Accession NM_005625) is another VGAM206 host target gene. SDCBP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDCBP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCBP BINDING SITE, designated SEQ ID:12137, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13275] Another function of VGAM206 is therefore inhibition of Syndecan Binding Protein (syntenin) (SDCBP, Accession NM_005625). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical

cal conditions associated with SDCBP. SEC24 Related Gene Family, Member D (*S. cerevisiae*) (SEC24D, Accession NM_014822) is another VGAM206 host target gene. SEC24D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC24D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC24D BINDING SITE, designated SEQ ID:16801, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13276] Another function of VGAM206 is therefore inhibition of SEC24 Related Gene Family, Member D (*S. cerevisiae*) (SEC24D, Accession NM_014822). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC24D. Septin 3 (SEPT3, Accession NM_019106) is another VGAM206 host target gene. SEPT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of SEPT3 BINDING SITE, designated SEQ ID:21186, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13277] Another function of VGAM206 is therefore inhibition of Septin 3 (SEPT3, Accession NM_019106). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPT3. SHC3 (Accession NM_016848) is another VGAM206 host target gene. SHC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SHC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SHC3 BINDING SITE, designated SEQ ID:18843, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13278] Another function of VGAM206 is therefore inhibition of SHC3 (Accession NM_016848). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SHC3. Solute Carrier Family 37 (glycerol-3-phosphate transporter),

Member 1 (SLC37A1, Accession NM_018964) is another VGAM206 host target gene. SLC37A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC37A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC37A1 BINDING SITE, designated SEQ ID:21035, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13279] Another function of VGAM206 is therefore inhibition of Solute Carrier Family 37 (glycerol-3-phosphate transporter), Member 1 (SLC37A1, Accession NM_018964). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC37A1. SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM_018450) is another VGAM206 host target gene. SMARCF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMARCF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of SMARCF1 BINDING SITE, designated SEQ ID:20523, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13280] Another function of VGAM206 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily F, Member 1 (SMARCF1, Accession NM_018450). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCF1. SR-BP1 (Accession NM_005866) is another VGAM206 host target gene. SR-BP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SR-BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SR-BP1 BINDING SITE, designated SEQ ID:12487, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13281] Another function of VGAM206 is therefore inhibition of SR-BP1 (Accession NM_005866). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SR-BP1. Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_139195) is another VGAM206 host target gene. ST7L BINDING SITE1 and ST7L BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7L BINDING SITE1 and ST7L BINDING SITE2, designated SEQ ID:29204 and SEQ ID:29209 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13282] Another function of VGAM206 is therefore inhibition of Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_139195). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7L. T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_012468) is another VGAM206 host target gene. TCL6 BINDING SITE1 and TCL6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCL6, corresponding to HOST TARGET binding sites such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCL6 BINDING SITE1 and TCL6 BINDING SITE2, designated SEQ ID:14848 and SEQ ID:20797 respectively, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13283] Another function of VGAM206 is therefore inhibition of T-cell Leukemia/lymphoma 6 (TCL6, Accession NM_012468). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCL6. TUSP (Accession NM_020245) is another VGAM206 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21534, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13284] Another function of VGAM206 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with TUSP.

LOC123242 (Accession XM_063548) is another VGAM206 host target gene. LOC123242 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123242, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123242 BINDING SITE, designated SEQ ID:37248, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13285] Another function of VGAM206 is therefore inhibition of LOC123242 (Accession XM_063548). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123242. LOC134637 (Accession XM_059727) is another VGAM206 host target gene. LOC134637 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC134637, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134637 BINDING SITE, designated SEQ ID:37080, to

the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13286] Another function of VGAM206 is therefore inhibition of LOC134637 (Accession XM_059727). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134637. LOC135398 (Accession XM_069333) is another VGAM206 host target gene. LOC135398 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135398, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135398 BINDING SITE, designated SEQ ID:37389, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13287] Another function of VGAM206 is therefore inhibition of LOC135398 (Accession XM_069333). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135398. LOC143308 (Accession XM_096411) is another VGAM206 host target gene. LOC143308 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC143308, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143308 BINDING SITE, designated SEQ ID:40350, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13288] Another function of VGAM206 is therefore inhibition of LOC143308 (Accession XM_096411). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143308. LOC144742 (Accession XM_084949) is another VGAM206 host target gene. LOC144742 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144742 BINDING SITE, designated SEQ ID:37780, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13289] Another function of VGAM206 is therefore inhibition of LOC144742 (Accession XM_084949). Accordingly, utilities

of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144742. LOC145945 (Accession XM_096908) is another VGAM206 host target gene. LOC145945 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145945 BINDING SITE, designated SEQ ID:40640, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13290] Another function of VGAM206 is therefore inhibition of LOC145945 (Accession XM_096908). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145945. LOC147632 (Accession NM_138478) is another VGAM206 host target gene. LOC147632 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC147632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC147632 BINDING SITE, designated SEQ ID:28829, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13291] Another function of VGAM206 is therefore inhibition of LOC147632 (Accession NM_138478). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147632. LOC147669 (Accession XM_097262) is another VGAM206 host target gene. LOC147669 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147669 BINDING SITE, designated SEQ ID:40855, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13292] Another function of VGAM206 is therefore inhibition of LOC147669 (Accession XM_097262). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147669. LOC149157 (Accession XM_086442) is another VGAM206 host target gene. LOC149157 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149157 BINDING SITE, designated SEQ ID:38658, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13293] Another function of VGAM206 is therefore inhibition of LOC149157 (Accession XM_086442). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149157. LOC149373 (Accession XM_086507) is another VGAM206 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38721, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13294] Another function of VGAM206 is therefore inhibition of

LOC149373 (Accession XM_086507). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC149935 (Accession XM_015885) is another VGAM206 host target gene. LOC149935 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149935, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149935 BINDING SITE, designated SEQ ID:30248, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13295] Another function of VGAM206 is therefore inhibition of LOC149935 (Accession XM_015885). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149935. LOC150157 (Accession XM_097823) is another VGAM206 host target gene. LOC150157 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150157 BINDING SITE, designated SEQ ID:41145, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13296] Another function of VGAM206 is therefore inhibition of LOC150157 (Accession XM_097823). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150157. LOC150271 (Accession XM_097859) is another VGAM206 host target gene. LOC150271 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150271, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150271 BINDING SITE, designated SEQ ID:41174, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13297] Another function of VGAM206 is therefore inhibition of LOC150271 (Accession XM_097859). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150271. LOC150279 (Accession XM_086820) is an-

other VGAM206 host target gene. LOC150279 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150279 BINDING SITE, designated SEQ ID:38902, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13298] Another function of VGAM206 is therefore inhibition of LOC150279 (Accession XM_086820). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150279. LOC150407 (Accession XM_086906) is another VGAM206 host target gene. LOC150407 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150407, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150407 BINDING SITE, designated SEQ ID:38955, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13299] Another function of VGAM206 is therefore inhibition of LOC150407 (Accession XM_086906). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150407. LOC152447 (Accession XM_087471) is another VGAM206 host target gene. LOC152447 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC152447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152447 BINDING SITE, designated SEQ ID:39274, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13300] Another function of VGAM206 is therefore inhibition of LOC152447 (Accession XM_087471). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152447. LOC153163 (Accession XM_087612) is another VGAM206 host target gene. LOC153163 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153163, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153163 BINDING SITE, designated SEQ ID:39361, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13301] Another function of VGAM206 is therefore inhibition of LOC153163 (Accession XM_087612). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153163. LOC158062 (Accession XM_098861) is another VGAM206 host target gene. LOC158062 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158062, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158062 BINDING SITE, designated SEQ ID:41915, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13302] Another function of VGAM206 is therefore inhibition of LOC158062 (Accession XM_098861). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC158062. LOC158292 (Accession XM_098914) is another VGAM206 host target gene. LOC158292 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158292 BINDING SITE, designated SEQ ID:41933, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13303] Another function of VGAM206 is therefore inhibition of LOC158292 (Accession XM_098914). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158292. LOC196283 (Accession XM_113684) is another VGAM206 host target gene. LOC196283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196283 BINDING SITE, designated SEQ ID:42343, to the nucleotide sequence of VGAM206 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2917.

[13304] Another function of VGAM206 is therefore inhibition of LOC196283 (Accession XM_113684). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196283. LOC196812 (Accession XM_116868) is another VGAM206 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43141, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13305] Another function of VGAM206 is therefore inhibition of LOC196812 (Accession XM_116868). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. LOC196890 (Accession XM_116951) is another VGAM206 host target gene. LOC196890 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196890, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196890 BINDING SITE, designated SEQ ID:43156, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13306] Another function of VGAM206 is therefore inhibition of LOC196890 (Accession XM_116951). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196890. LOC200035 (Accession XM_055305) is another VGAM206 host target gene. LOC200035 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200035 BINDING SITE, designated SEQ ID:36264, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13307] Another function of VGAM206 is therefore inhibition of LOC200035 (Accession XM_055305). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC200035. LOC201229 (Accession XM_113925) is another VGAM206 host target gene. LOC201229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201229 BINDING SITE, designated SEQ ID:42546, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13308] Another function of VGAM206 is therefore inhibition of LOC201229 (Accession XM_113925). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201229. LOC201252 (Accession XM_113941) is another VGAM206 host target gene. LOC201252 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201252, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201252 BINDING SITE, designated SEQ ID:42557, to

the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13309] Another function of VGAM206 is therefore inhibition of LOC201252 (Accession XM_113941). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201252. LOC204285 (Accession XM_115292) is another VGAM206 host target gene. LOC204285 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204285 BINDING SITE, designated SEQ ID:43091, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13310] Another function of VGAM206 is therefore inhibition of LOC204285 (Accession XM_115292). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204285. LOC204970 (Accession XM_114795) is another VGAM206 host target gene. LOC204970 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC204970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204970 BINDING SITE, designated SEQ ID:43074, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13311] Another function of VGAM206 is therefore inhibition of LOC204970 (Accession XM_114795). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204970. LOC219654 (Accession XM_166095) is another VGAM206 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219654 BINDING SITE, designated SEQ ID:43873, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13312] Another function of VGAM206 is therefore inhibition of LOC219654 (Accession XM_166095). Accordingly, utilities

of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC220064 (Accession XM_167827) is another VGAM206 host target gene. LOC220064 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220064 BINDING SITE, designated SEQ ID:44871, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13313] Another function of VGAM206 is therefore inhibition of LOC220064 (Accession XM_167827). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220064. LOC221025 (Accession XM_167644) is another VGAM206 host target gene. LOC221025 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221025, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221025 BINDING SITE, designated SEQ ID:44747, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13314] Another function of VGAM206 is therefore inhibition of LOC221025 (Accession XM_167644). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221025. LOC221794 (Accession XM_168214) is another VGAM206 host target gene. LOC221794 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221794 BINDING SITE, designated SEQ ID:45072, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13315] Another function of VGAM206 is therefore inhibition of LOC221794 (Accession XM_168214). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221794. LOC222256 (Accession XM_168571) is another VGAM206 host target gene. LOC222256 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222256, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222256 BINDING SITE, designated SEQ ID:45251, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13316] Another function of VGAM206 is therefore inhibition of LOC222256 (Accession XM_168571). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222256. LOC222614 (Accession XM_169970) is another VGAM206 host target gene. LOC222614 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222614, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222614 BINDING SITE, designated SEQ ID:45307, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13317] Another function of VGAM206 is therefore inhibition of

LOC222614 (Accession XM_169970). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222614. LOC222962 (Accession XM_167291) is another VGAM206 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44632, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13318] Another function of VGAM206 is therefore inhibition of LOC222962 (Accession XM_167291). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. LOC253001 (Accession XM_171711) is another VGAM206 host target gene. LOC253001 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC253001 BINDING SITE, designated SEQ ID:46062, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13319] Another function of VGAM206 is therefore inhibition of LOC253001 (Accession XM_171711). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253001. LOC253639 (Accession XM_171060) is another VGAM206 host target gene. LOC253639 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253639 BINDING SITE, designated SEQ ID:45857, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13320] Another function of VGAM206 is therefore inhibition of LOC253639 (Accession XM_171060). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253639. LOC254381 (Accession XM_173436) is an-

other VGAM206 host target gene. LOC254381 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC254381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254381 BINDING SITE, designated SEQ ID:46545, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13321] Another function of VGAM206 is therefore inhibition of LOC254381 (Accession XM_173436). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254381. LOC254423 (Accession XM_173286) is another VGAM206 host target gene. LOC254423 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC254423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254423 BINDING SITE, designated SEQ ID:46532, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13322] Another function of VGAM206 is therefore inhibition of LOC254423 (Accession XM_173286). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254423. LOC255452 (Accession XM_174088) is another VGAM206 host target gene. LOC255452 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255452, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255452 BINDING SITE, designated SEQ ID:46578, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13323] Another function of VGAM206 is therefore inhibition of LOC255452 (Accession XM_174088). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255452. LOC256520 (Accession XM_171126) is another VGAM206 host target gene. LOC256520 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256520, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256520 BINDING SITE, designated SEQ ID:45929, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13324] Another function of VGAM206 is therefore inhibition of LOC256520 (Accession XM_171126). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256520. LOC257104 (Accession XM_173830) is another VGAM206 host target gene. LOC257104 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257104, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257104 BINDING SITE, designated SEQ ID:46564, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13325] Another function of VGAM206 is therefore inhibition of LOC257104 (Accession XM_173830). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC257104. LOC257282 (Accession XM_172844) is another VGAM206 host target gene. LOC257282 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257282, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257282 BINDING SITE, designated SEQ ID:46122, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13326] Another function of VGAM206 is therefore inhibition of LOC257282 (Accession XM_172844). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257282. LOC91409 (Accession XM_038298) is another VGAM206 host target gene. LOC91409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91409 BINDING SITE, designated SEQ ID:32806, to the nucleotide sequence of VGAM206 RNA, herein designated

VGAM RNA, also designated SEQ ID:2917.

[13327] Another function of VGAM206 is therefore inhibition of LOC91409 (Accession XM_038298). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91409. LOC91828 (Accession XM_040910) is another VGAM206 host target gene. LOC91828 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91828 BINDING SITE, designated SEQ ID:33410, to the nucleotide sequence of VGAM206 RNA, herein designated VGAM RNA, also designated SEQ ID:2917.

[13328] Another function of VGAM206 is therefore inhibition of LOC91828 (Accession XM_040910). Accordingly, utilities of VGAM206 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91828. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 207 (VGAM207) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13329] VGAM207 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM207 was detected is described hereinabove with reference to Figs. 1–8.

[13330] VGAM207 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13331] VGAM207 gene encodes a VGAM207 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM207 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM207 precursor RNA is designated SEQ ID:193, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:193 is located at position 203744 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13332] VGAM207 precursor RNA folds onto itself, forming VGAM207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13333] An enzyme complex designated DICER COMPLEX, `dices` the VGAM207 folded precursor RNA into VGAM207 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM207 RNA is designated SEQ ID:2918, and is provided hereinbelow with reference to the sequence listing part.

[13334] VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM207 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM207 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13335] VGAM207 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM207 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM207 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13336] The complementary binding of VGAM207 RNA, herein designated VGAM RNA, to host target binding sites on VGAM207 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM207 host target RNA into VGAM207 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13337] It is appreciated that VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM207 host target genes. The mRNA of each one of this plurality of VGAM207 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM207 RNA, herein designated VGAM RNA, and which when bound by VGAM207 RNA causes inhibition of translation of respective one or more VGAM207 host target proteins.

[13338] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM207 gene, herein designated VGAM GENE, on one or more VGAM207 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13339] It is yet further appreciated that a function of VGAM207 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM207 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM207 correlate

with, and may be deduced from, the identity of the host target genes which VGAM207 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13340] Nucleotide sequences of the VGAM207 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM207 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM207 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM207 are further described hereinbelow with reference to Table 1.

[13341] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM207 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM207 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13342] As mentioned hereinabove with reference to Fig. 1, a function of VGAM207 gene, herein designated VGAM is inhibition of expression of VGAM207 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM207 correlate with, and may be deduced

from, the identity of the target genes which VGAM207 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13343] Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Accession NM_025136) is a VGAM207 host target gene. OPA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA3 BINDING SITE, designated SEQ ID:24776, to the nucleotide sequence of VGAM207 RNA, herein designated VGAM RNA, also designated SEQ ID:2918.

[13344] A function of VGAM207 is therefore inhibition of Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Accession NM_025136). Accordingly, utilities of VGAM207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA3. LOC159184 (Accession XM_010658) is another VGAM207 host target gene. LOC159184 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC159184, corresponding

to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159184 BINDING SITE, designated SEQ ID:30162, to the nucleotide sequence of VGAM207 RNA, herein designated VGAM RNA, also designated SEQ ID:2918.

[13345] Another function of VGAM207 is therefore inhibition of LOC159184 (Accession XM_010658). Accordingly, utilities of VGAM207 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159184. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 208 (VGAM208) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13346] VGAM208 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM208 was detected is described hereinabove with reference to Figs. 1–8.

[13347] VGAM208 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syn–

drome Virus (white spot bacilliform virus). VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13348] VGAM208 gene encodes a VGAM208 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM208 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM208 precursor RNA is designated SEQ ID:194, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:194 is located at position 15808 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13349] VGAM208 precursor RNA folds onto itself, forming VGAM208 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13350] An enzyme complex designated DICER COMPLEX, `dices` the VGAM208 folded precursor RNA into VGAM208 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 57%) nucleotide sequence of VGAM208 RNA is designated SEQ ID:2919, and is provided hereinbelow with reference to the sequence listing part.

[13351] VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM208 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13352] VGAM208 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM208 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM208 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13353] The complementary binding of VGAM208 RNA, herein designated VGAM RNA, to host target binding sites on VGAM208 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM208 host tar-

get RNA into VGAM208 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13354] It is appreciated that VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM208 host target genes. The mRNA of each one of this plurality of VGAM208 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM208 RNA, herein designated VGAM RNA, and which when bound by VGAM208 RNA causes inhibition of translation of respective one or more VGAM208 host target proteins.

[13355] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM208 gene, herein designated VGAM GENE, on one or more VGAM208 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13356] It is yet further appreciated that a function of VGAM208 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM208 correlate with, and may be deduced from, the identity of the host target genes which VGAM208 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13357] Nucleotide sequences of the VGAM208 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM208 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM208 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM208 are further described hereinbelow with reference to Table 1.

[13358] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM208 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM208 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13359] As mentioned hereinabove with reference to Fig. 1, a function of VGAM208 gene, herein designated VGAM is inhibition of expression of VGAM208 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM208 correlate with, and may be deduced from, the identity of the target genes which VGAM208 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13360] Activin A Receptor, Type IB (ACVR1B, Accession NM_004302) is a VGAM208 host target gene. ACVR1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACVR1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of ACVR1B BINDING SITE, designated SEQ ID:10511, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13361] A function of VGAM208 is therefore inhibition of Activin A Receptor, Type IB (ACVR1B, Accession NM_004302), a gene which Activin receptor-like kinase; similar to activin, TGF-beta, and C. elegans daf-1 receptors. Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACVR1B. The function of ACVR1B has been established by previous studies. See ACVRL1 (OMIM Ref. No. 601284). Human cDNA clones encoding 4 putative trans-membrane ser/thr kinases were identified by ten Dijke et al. (1993). Using degenerate DNA primers based on the human activin receptor type II (see OMIM Ref. No. 102581) and C. elegans Daf-1 gene products, they PCR-amplified mRNA from human erythroleukemia (HEL) cells, a cell type known to respond both to activin (OMIM Ref. No. 147290) and TGF-beta (OMIM Ref. No. 190180). Their partial clone of the ALK4 gene encodes a 383-amino acid polypeptide with a truncated extracellular domain but sequence and

structural domain similarities with the other 3 ALK genes they cloned. ALK1, ALK2 (OMIM Ref. No. 102576), ALK3 (OMIM Ref. No. 601299), and ALK4 share approximately 40% sequence identity with activin receptors type II and IIB, TGF-beta receptor (see OMIM Ref. No. 190181), and Daf-1 in their kinase domains but share 60 to 79% sequence identity among themselves, suggesting to ten Dijke et al. (1993) that the ALK gene products form a subfamily of receptor ser/thr kinases. By Northern analysis, ten Dijke et al. (1993) showed that ALK4 is expressed in many tissues, most strongly in human kidney, pancreas, brain, lung, and liver. Su et al. (2001) described the gene structure and novel somatic mutations of the activin type IB receptor in pancreatic cancer. This was the first description of ACVR1B as a tumor suppressor gene.

[13362] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13363] ten Dijke, P.; Ichijo, H.; Franzen, P.; Schulz, P.; Saras, J.; Toyoshima, H.; Heldin, C.-H.; Miyazono, K. : Activin receptor-like kinases: a novel subclass of cell-surface receptors with predicted serine/threonine kinase activity. *Oncogene* 8: 2879-2887, 1993. ; and

[13364] Su, G. H.; Bansal, R.; Murphy, K. M.; Montgomery, E.; Yeo, C. J.; Hruban, R. H.; Kern, S. E. : ACVR1B (ALK4, activin receptor type 1B) gene mutations in pancreatic carcinoma. Proc. Nat.

[13365] Further studies establishing the function and utilities of ACVR1B are found in John Hopkins OMIM database record ID 601300, and in cited publications numbered 6501, 650 and 6503–6504 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Kinesin Family Member 3C (KIF3C, Accession NM_002254) is another VGAM208 host target gene. KIF3C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIF3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3C BINDING SITE, designated SEQ ID:8056, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13366] Another function of VGAM208 is therefore inhibition of Kinesin Family Member 3C (KIF3C, Accession NM_002254). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clini–

cal conditions associated with KIF3C. Adaptor-related Protein Complex 3, Sigma 2 Subunit (AP3S2, Accession NM_005829) is another VGAM208 host target gene. AP3S2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by AP3S2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP3S2 BINDING SITE, designated SEQ ID:12438, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13367] Another function of VGAM208 is therefore inhibition of Adaptor-related Protein Complex 3, Sigma 2 Subunit (AP3S2, Accession NM_005829). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP3S2. DRIL2 (Accession NM_006465) is another VGAM208 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ

ID:13183, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13368] Another function of VGAM208 is therefore inhibition of DRIL2 (Accession NM_006465). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. FLJ23311 (Accession NM_024680) is another VGAM208 host target gene. FLJ23311 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ23311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23311 BINDING SITE, designated SEQ ID:23992, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13369] Another function of VGAM208 is therefore inhibition of FLJ23311 (Accession NM_024680). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23311. KIAA0193 (Accession NM_014766) is another VGAM208 host target gene. KIAA0193 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16539, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13370] Another function of VGAM208 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. MGC4172 (Accession NM_024308) is another VGAM208 host target gene. MGC4172 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4172, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4172 BINDING SITE, designated SEQ ID:23601, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13371] Another function of VGAM208 is therefore inhibition of

MGC4172 (Accession NM_024308). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4172. LOC112609 (Accession XM_053013) is another VGAM208 host target gene. LOC112609 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112609 BINDING SITE, designated SEQ ID:36058, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13372] Another function of VGAM208 is therefore inhibition of LOC112609 (Accession XM_053013). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112609. LOC196484 (Accession XM_031807) is another VGAM208 host target gene. LOC196484 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196484, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC196484 BINDING SITE, designated SEQ ID:31485, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13373] Another function of VGAM208 is therefore inhibition of LOC196484 (Accession XM_031807). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196484. LOC220073 (Accession XM_167847) is another VGAM208 host target gene. LOC220073 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220073, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220073 BINDING SITE, designated SEQ ID:44873, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13374] Another function of VGAM208 is therefore inhibition of LOC220073 (Accession XM_167847). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220073. LOC91069 (Accession XM_035824) is an-

other VGAM208 host target gene. LOC91069 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91069, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91069 BINDING SITE, designated SEQ ID:32345, to the nucleotide sequence of VGAM208 RNA, herein designated VGAM RNA, also designated SEQ ID:2919.

[13375] Another function of VGAM208 is therefore inhibition of LOC91069 (Accession XM_035824). Accordingly, utilities of VGAM208 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91069. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 209 (VGAM209) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13376] VGAM209 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM209 was detected is described

hereinabove with reference to Figs. 1–8.

[13377] VGAM209 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13378] VGAM209 gene encodes a VGAM209 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM209 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM209 precursor RNA is designated SEQ ID:195, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:195 is located at position 72618 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13379] VGAM209 precursor RNA folds onto itself, forming VGAM209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13380] An enzyme complex designated DICER COMPLEX, `dices` the VGAM209 folded precursor RNA into VGAM209 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 65%) nucleotide sequence of VGAM209 RNA is designated SEQ ID:2920, and is provided hereinbelow with reference to the sequence listing part.

[13381] VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM209 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13382] VGAM209 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM209 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM209 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[13383] The complementary binding of VGAM209 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM209 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM209 host target RNA into VGAM209 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13384] It is appreciated that VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM209 host target genes. The mRNA of each one of this plurality of VGAM209 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM209 RNA, herein designated VGAM RNA, and which when bound by VGAM209 RNA causes inhibition of translation of respective one or more VGAM209 host target proteins.

[13385] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM209 gene, herein designated VGAM GENE, on one or more VGAM209 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13386] It is yet further appreciated that a function of VGAM209 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM209 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM209 correlate with, and may be deduced from, the identity of the host target genes which VGAM209 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13387] Nucleotide sequences of the VGAM209 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM209 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM209 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM209 are further described hereinbelow with reference to Table 1.

[13388] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM209 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM209 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13389] As mentioned hereinabove with reference to Fig. 1, a function of VGAM209 gene, herein designated VGAM is inhibition of expression of VGAM209 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM209 correlate with, and may be deduced from, the identity of the target genes which VGAM209 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13390] Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876) is a VGAM209 host target gene. IGF2R BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by IGF2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2R BINDING SITE, designated SEQ ID:6560, to the nucleotide sequence of VGAM209 RNA, herein designated VGAM RNA, also designated SEQ ID:2920.

[13391] A function of VGAM209 is therefore inhibition of Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876), a gene which transport of phosphorylated lysosomal enzymes from the golgi complex and the cell surface to lysosomes. lysosomal enzymes bearing phosphomannosyl residues bind specifically to mannose-6-phosphate receptors in the golgi apparatus and the resulting receptor-ligand complex is transported to an acidic prelysosomal compartment where the low ph mediates the dissociation of the complex. this receptor also binds insulin growth factor ii. Accordingly, utilities of VGAM209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2R. The function of IGF2R has been established by previous studies. The mannose 6-phosphate/insulin-like growth factor II receptor functions in the intracellular trafficking

of lysosomal enzymes, the activation of the potent growth inhibitor, transforming growth factor beta, and the degradation of IGF2, a mitogen often overproduced in tumors. De Souza et al. (1995) demonstrated that 70% of human hepatocellular tumors have loss of heterozygosity (LOH) at the M6P/IGF2R locus at 6q26. In a separate report, De Souza et al. (1995) described a mutation screen that identified point mutations in the remaining allele of 25% of human hepatocellular carcinomas with LOH. One mutation created an alternative splice site within an intron (corresponding to intron 40 in mouse) and resulted in a truncated receptor; 2 others (147280.0001, 147280.0002) gave rise to significant amino acid substitutions. These mutations provided evidence to the authors that the M6P/IGF2R gene functions as a tumor suppressor in human liver carcinogenesis. Souza et al. (1996) reported that the IGF2R gene contains a number of microsatellite repeats within its coding sequence. They demonstrated microsatellite instability in this gene in 12 of 92 gastrointestinal tumors studied which were replication/repair error-positive. Mutations occurred in 6 of the poorly differentiated tumors. They noted an anticorrespondence of IGF2R and TGFBR2 (OMIM Ref. No. 190182)

mutations. Of 31 gastrointestinal lesions studied with IGF2R or TGFBR2 mutations, 90% (28) contained mutations in one or the other, but not both, of these genes. Souza et al. (1996) demonstrated that all but 1 of the mutations occurred within an 8-polydeoxyguanine tract spanning nucleotides 4089–4096 of the IGF2R coding sequence. In 1 case of gastric adenocarcinoma, mutation occurred in a polyCT tract spanning nucleotides 6169–6180. These mutations all comprised 1- or 2-bp deletions or insertions within the microsatellite region, causing frameshifts and premature stop codons downstream. Souza et al. (1996) noted that the TGFBR2 gene is also subject to microsatellite instability within its coding region. They noted further that IGF2R and TGFBR2 genes comprise serial points in the same tumorigenesis pathway, since mutation of either gene alone occurred in 90% of the gastrointestinal tumors that they analyzed. To facilitate genetic analyses of the imprint status of human M6P/IGF2R and loss of heterozygosity at this locus in cancer, Killian et al. (2001) screened American and Japanese populations for M6P/IGF2R single nucleotide polymorphisms (SNPs). They identified 9 novel intragenic SNPs and 3 amino acid variants in the ligand-binding domains of M6P/IGF2R that may be under selec-

tion in humans Animal model experiments lend further support to the function of IGF2R. To determine whether paternal expression of the Igf2r gene is necessary for early development in the mouse, Lau et al. (1994) derived mice in which the gene had been disrupted by targeted mutagenesis in embryonic stem (ES) cells with the subsequent introduction of the mutation into the germline of mice. Lau et al. (1994) found that murine embryos that inherit a nonfunctional Igf2r gene from their father are viable and develop normally into adults; however, most mice inheriting the same mutated allele from their mothers die around the time of birth as a consequence of major cardiac abnormalities. The mice that inherit the mutant allele from their mothers do not express Igf2r in their tissues, are 25 to 30% larger than their normal sibs, have elevated levels of circulating IGF2 and IGF-binding proteins, and exhibit a slight kink in the tail. The findings of overgrowth may support the suggestion that relaxation of maternal imprinting of IGF2 plays a role in the features of Beckwith-Wiedemann syndrome (OMIM Ref. No. 130650) (Feinberg, 1993).

[13392] It is appreciated that the abovementioned animal model for IGF2R is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13393] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13394] Lau, M. M. H.; Stewart, C. E. H.; Liu, Z.; Bhatt, H.; Rotwein, P.; Stewart, C. L. : Loss of the imprinted IGF2/cation-independent mannose 6-phosphate receptor results in fetal overgrowth and perinatal lethality. *Genes Dev.* 8: 2953–2963, 1994. ; and

[13395] Sleutels, F.; Zwart, R.; Barlow, D. P. : The non-coding Air RNA is required for silencing autosomal imprinted genes. *Nature* 415: 810–813, 2002.

[13396] Further studies establishing the function and utilities of IGF2R are found in John Hopkins OMIM database record ID 147280, and in cited publications numbered 4824–4839, 470 and 5228–5240 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neural Precursor Cell Expressed, Developmentally Down-regulated 4 (NEDD4, Accession XM_046129) is another VGAM209 host target gene. NEDD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEDD4, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEDD4 BINDING SITE, designated SEQ ID:34692, to the nucleotide sequence of VGAM209 RNA, herein designated VGAM RNA, also designated SEQ ID:2920.

[13397] Another function of VGAM209 is therefore inhibition of Neural Precursor Cell Expressed, Developmentally Down-regulated 4 (NEDD4, Accession XM_046129), a gene which ubiquitinates regulatory proteins involved in transcription. Accordingly, utilities of VGAM209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEDD4. The function of NEDD4 has been established by previous studies. Kumar et al. (1992) identified Nedd4 as one of a group of mouse genes that show developmentally regulated expression in mouse embryonic brain. Kumar et al. (1997) showed that Nedd4 is expressed in various other embryonic tissues and persists in most adult tissues. Using antibody raised against a fusion protein, they demonstrated that the Nedd4 protein is localized to the cellular cytoplasm. Kumar et al. (1997) reported that the human NEDD4 protein has 86% amino acid identity with the mouse protein. It has homology to ubiq-

ubiquitin–protein ligases and contains 4 protein–protein interaction (WW) domains and a calcium/phospholipid binding domain. Imhof and McDonnell (1996) found that both human NEDD4 and yeast RSP5 potentiate hormone–dependent activation of transcription by the human progesterone and glucocorticoid receptors. They used mutant proteins to show that neither the ubiquitin–protein ligase activity nor the WW domains are absolutely required for the potentiation of the steroid receptors.

[13398] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13399] Imhof, M. O.; McDonnell, D. P. : Yeast RSP5 and its human homolog hRPF1 potentiate hormone–dependent activation of transcription by human progesterone and glucocorticoid receptors. *Molec. Cell. Biol.* 16: 2594–2605, 1996. ; and

[13400] Kumar, S.; Harvey, K. F.; Kinoshita, M.; Copeland, N. G.; Noda, M.; Jenkins, N. A. : cDNA cloning, expression analysis, and mapping of the mouse Nedd4 gene. *Genomics* 40: 435–443, 1997.

[13401] Further studies establishing the function and utilities of NEDD4 are found in John Hopkins OMIM database record

ID 602278, and in cited publications numbered 7555–280 and 1596 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAD17 Homolog (*S. pombe*) (RAD17, Accession NM_133340) is another VGAM209 host target gene. RAD17 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAD17, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD17 BINDING SITE, designated SEQ ID:28481, to the nucleotide sequence of VGAM209 RNA, herein designated VGAM RNA, also designated SEQ ID:2920.

[13402] Another function of VGAM209 is therefore inhibition of RAD17 Homolog (*S. pombe*) (RAD17, Accession NM_133340), a gene which may have a role in DNA damage-dependent and DNA replication-dependent cell cycle checkpoints. Accordingly, utilities of VGAM209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD17. The function of RAD17 has been established by previous studies. Cell cycle checkpoints are complex signal transduction pathways that ensure the coordination of the timing and order of

cell cycle events. These checkpoint pathways play critical roles in maintaining genomic stability and integrity to prevent the development of cancer and hereditary diseases. In the fission yeast *Schizosaccharomyces pombe*, the *rad17* gene is required for both the DNA damage-dependent and the DNA replication-dependent cell cycle checkpoints. Parker et al. (1998) identified expressed sequence tags corresponding to a human homolog of *S. pombe rad17*. By PCR, they isolated a human SK-N-MC neuroblastoma cell cDNA containing the complete open reading frame of this homolog, RAD17. The deduced 670-amino acid RAD17 protein has a calculated molecular mass of 71 kD and has 20% sequence identity to *S. pombe rad17*. Northern blot analysis detected an approximately 3.0-kb transcript in all tissues examined, with elevated levels in testis and cancer cell lines. Although human RAD17 did not complement the checkpoint phenotypes of an *S. pombe rad17* mutant, it interacted with human RAD1 (OMIM Ref. No. 603153) in a yeast 2-hybrid system, and Parker et al. (1998) suggested that it is the homolog of *S. pombe rad17*.

[13403] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [13404] Parker, A. E.; Van de Weyer, I.; Laus, M. C.; Verhasselt, P.; Luyten, W. H. M. L. : Identification of a human homologue of the *Schizosaccharomyces pombe* rad17+ checkpoint gene. *J. Biol. Chem.* 273: 18340–18346, 1998. Note: Erratum: *J. Biol. Chem.* 274: 24438–24439, 1999. ; and
- [13405] Bao, S.; Tibbetts, R. S.; Brumbaugh, K. M.; Fang, Y.; Richardson, D. A.; Ali, A.; Chen, S. M.; Abraham, R. T.; Wang, X.-F. : ATR/ATM-mediated phosphorylation of human Rad17 is required f.
- [13406] Further studies establishing the function and utilities of RAD17 are found in John Hopkins OMIM database record ID 603139, and in cited publications numbered 5065, 1010 and 5423–5424 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BC022889 (Accession XM_096964) is another VGAM209 host target gene. BC022889 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BC022889, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BC022889 BINDING SITE, designated SEQ ID:40685, to the

nucleotide sequence of VGAM209 RNA, herein designated VGAM RNA, also designated SEQ ID:2920.

[13407] Another function of VGAM209 is therefore inhibition of BC022889 (Accession XM_096964). Accordingly, utilities of VGAM209 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BC022889. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 210 (VGAM210) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13408] VGAM210 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM210 was detected is described hereinabove with reference to Figs. 1–8.

[13409] VGAM210 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus). VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13410] VGAM210 gene encodes a VGAM210 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM210 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM210 precursor RNA is designated SEQ ID:196, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:196 is located at position 58881 relative to the genome of Shrimp White Spot Syndrome Virus (white spot bacilliform virus).

[13411] VGAM210 precursor RNA folds onto itself, forming VGAM210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13412] An enzyme complex designated DICER COMPLEX, `dices` the VGAM210 folded precursor RNA into VGAM210 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM210 RNA is designated SEQ ID:2921, and is provided hereinbelow with reference to the sequence listing part.

[13413] VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM210 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13414] VGAM210 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM210 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM210 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[13415] The complementary binding of VGAM210 RNA, herein designated VGAM RNA, to host target binding sites on VGAM210 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM210 host target RNA into VGAM210 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13416] It is appreciated that VGAM210 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM210 host target genes. The mRNA of each one of this plurality of VGAM210 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM210 RNA, herein designated VGAM RNA, and which when bound by VGAM210 RNA causes inhibition of translation of respective one or more VGAM210 host target proteins.

[13417] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM210 gene, herein designated VGAM GENE, on one or more VGAM210 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13418] It is yet further appreciated that a function of VGAM210 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of viral infection by Shrimp White Spot Syndrome Virus (white spot bacilliform virus). Specific functions, and accordingly utilities, of VGAM210 correlate with, and may be deduced from, the identity of the host target genes which VGAM210 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13419] Nucleotide sequences of the VGAM210 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM210 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM210 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM210 are further described hereinbelow with reference to Table 1.

[13420] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM210 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM210 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13421] As mentioned hereinabove with reference to Fig. 1, a function of VGAM210 gene, herein designated VGAM is inhibition of expression of VGAM210 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM210 correlate with, and may be deduced from, the identity of the target genes which VGAM210 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13422] Cadherin 3, Type 1, P-cadherin (placental) (CDH3, Accession NM_001793) is a VGAM210 host target gene. CDH3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH3 BINDING SITE, designated SEQ ID:7545, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13423] A function of VGAM210 is therefore inhibition of Cadherin 3, Type 1, P-cadherin (placental) (CDH3, Accession NM_001793), a gene which is a calcium dependent cell adhesion protein. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH3. The function of CDH3 has been established by previous studies. Cadherins are a multigene family of $\text{Ca}(2+)$ -dependent cell adhesion molecules. They are transmembrane glycoproteins consisting of an extracellular domain, a transmembrane region, and a cytoplasmic domain. The extracellular domains mediate $\text{Ca}(2+)$ -dependent intercellular adhesion by homophilic interactions. The binding properties and specificities of the adhesive function are located in the N-terminal part of the molecules. Neural (OMIM Ref. No. 114020), placental (OMIM Ref. No. 114021), and epithelial (also called uvomorulin; 192090) forms of cadherin have been characterized. Donalies et al. (1991) identified a member of the cadherin family in myogenic mouse cells and referred to it as M-cadherin. It was not found in fibroblasts and was expressed at low levels in myoblasts. It is upregulated after induction of myotube formation, indicating a specific function in skeletal muscle

cell differentiation. Kaupmann et al. (1992) used a mouse myotube-derived cDNA encoding M-cadherin to demonstrate linkage of the gene (symbolized Cdh3 by them) to the gene for E-cadherin (uvomorulin; Um) in a mouse interspecific backcross. The linkage group is located on chromosome 8 in a region of conserved synteny with human chromosome 16q. The gene order was centromere--Junb--Um--Tat--(Cdh3/Aprt). The human homolog, symbolized CDH3 by them, was mapped to 16q24.1-qter by analyzing human/mouse somatic cell hybrids. Kremmidiotis et al. (1998) mapped the human CDH15 gene to 16q24.3 using somatic cell hybrid panels.

[13424] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13425] Donalies, M.; Cramer, M.; Ringwald, M.; Starzinski-Powitz, A. : Expression of M-cadherin, a member of the cadherin multigene family, correlates with differentiation of skeletal muscle cells. Proc. Nat. Acad. Sci. 88: 8024-8028, 1991. ; and

[13426] Kaupmann, K.; Becker-Follmann, J.; Scherer, G.; Jockusch, H.; Starzinski-Powitz, A. : The gene for the cell adhesion molecule M-cadherin maps to mouse chromosome 8 and

human chromosome.

[13427] Further studies establishing the function and utilities of CDH3 are found in John Hopkins OMIM database record ID 114019, and in cited publications numbered 11644–11646 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_001396) is another VGAM210 host target gene. DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DYRK1A, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYRK1A BINDING SITE1 through DYRK1A BINDING SITE3, designated SEQ ID:7092, SEQ ID:28160 and SEQ ID:28185 respectively, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13428] Another function of VGAM210 is therefore inhibition of Dual-specificity tyrosine-(Y)-phosphorylation Regulated Kinase 1A (DYRK1A, Accession NM_001396), a gene which regulates cell proliferation and may be involved in brain

development . Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYRK1A. The function of DYRK1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM42. Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962) is another VGAM210 host target gene. IL22RA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL22RA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL22RA2 BINDING SITE, designated SEQ ID:27521, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13429] Another function of VGAM210 is therefore inhibition of Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962), a gene which induces the production of acute-phase reactants. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL22RA2. The func-

tion of IL22RA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167. Jerky Homolog (mouse) (JRK, Accession XM_098818) is another VGAM210 host target gene. JRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JRK BINDING SITE, designated SEQ ID:41834, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13430] Another function of VGAM210 is therefore inhibition of Jerky Homolog (mouse) (JRK, Accession XM_098818), a gene which might function as a DNA-binding protein. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JRK. The function of JRK has been established by previous studies. Toth et al. (1995) found that insertional inactivation of the mouse 'jerky' gene resulted in handling-induced whole body jerks, generalized clonic seizures, and epileptic brain activity. All homozygous ani-

mals displayed seizures. Homozygotes also displayed some degree of kyphosis of the thoracic spine and were proportionate dwarfs. Approximately half died before 3 months of age. Approximately 50% of the hemizygous animals showed generalized clonic seizures. The other hemizygous animals either displayed seizures limited to the head and limbs or showed no seizure activity. There was no apparent correlation between the level of jerky mRNA and the severity of seizures in hemizygotes. Toth et al. (1995) reported the sequence of jerky and a corrected version in a published erratum. The predicted protein has homology to several nuclear regulatory proteins, including CENPB (OMIM Ref. No. 117140), suggesting that jerky might function as a DNA-binding protein. By searching an EST database, Morita et al. (1998) identified a human infant brain cDNA encoding JH8 (jerky homolog of human on chromosome 8). Using this cDNA as a probe, they recovered additional clones corresponding to the entire JH8 coding region. The predicted 520-amino acid protein shares 76% and 41% sequence identity with jerky and HH-MJG (OMIM Ref. No. 603211), respectively. Northern blot analysis revealed that JH8 is expressed as a 9.5-kb mRNA in all tissues. Additional smaller bands were also detected.

Toth et al. (1995) mapped the jerky gene to mouse chromosome 15 by analysis of an interspecific backcross. By fluorescence in situ hybridization and analysis of a radiation hybrid panel, Morita et al. (1998) mapped the JH8 gene to 8q24. The mouse chromosome region containing jerky shows homology of synteny with human chromosome 8q24, suggesting that JH8, rather than HHMJG, is the human homolog of jerky. Morita et al. (1998) considered JH8 a prominent candidate gene for childhood absence epilepsy-1 (OMIM Ref. No. 600131), which maps to 8q24.

[13431] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13432] Morita, R.; Miyazaki, E.; Fong, C. G.; Chen, X.-N.; Korenberg, J. R.; Delgado-Escueta, A. V.; Yamakawa, K. : JH8, a gene highly homologous to the mouse jerky gene, maps to the region for childhood absence epilepsy on 8q24. Biochem. Biophys. Res. Commun. 248: 307-314, 1998. ; and

[13433] Toth, M.; Grimsby, J.; Buzsaki, G.; Donovan, G. P. : Epileptic seizures caused by inactivation of a novel gene, jerky, related to centromere binding protein-B in transgenic

mice. Nature.

[13434] Further studies establishing the function and utilities of JRK are found in John Hopkins OMIM database record ID 603210, and in cited publications numbered 5437–5438 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198) is another VGAM210 host target gene. PDK4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDK4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDK4 BINDING SITE, designated SEQ ID:46444, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13435] Another function of VGAM210 is therefore inhibition of Pyruvate Dehydrogenase Kinase, Isoenzyme 4 (PDK4, Accession XM_173198). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDK4. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558) is another VGAM210 host target

gene. PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PPP1R8, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE1 through PPP1R8 BINDING SITE3, designated SEQ ID:28858, SEQ ID:15342 and SEQ ID:8572 respectively, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13436] Another function of VGAM210 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM101.SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1

(SMARCD1, Accession NM_003076) is another VGAM210 host target gene. SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SMARCD1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMARCD1 BINDING SITE1 and SMARCD1 BINDING SITE2, designated SEQ ID:9049 and SEQ ID:29147 respectively, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13437] Another function of VGAM210 is therefore inhibition of SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily D, Member 1 (SMARCD1, Accession NM_003076), a gene which is involved in chromatin assembly and remodeling. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMARCD1. The function of SMARCD1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession

NM_003242) is another VGAM210 host target gene.

TGFBR2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TGFBR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFBR2 BINDING SITE, designated SEQ ID:9241, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13438] Another function of VGAM210 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFBR2, Accession NM_003242). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR2. Thymidine Kinase 2, Mitochondrial (TK2, Accession NM_004614) is another VGAM210 host target gene. TK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TK2 BINDING SITE, designated SEQ ID:10958, to the nu-

cleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13439] Another function of VGAM210 is therefore inhibition of Thymidine Kinase 2, Mitochondrial (TK2, Accession NM_004614), a gene which phosphorylates thymidine, deoxycytidine, deoxyuridine, and also anti-viral and anti-cancer nucleoside analogs. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TK2. The function of TK2 has been established by previous studies. Johansson and Karlsson (1997) cloned cDNAs encoding human TK2. The gene encodes a 234-amino acid polypeptide. Although TK2 is believed to reside in mitochondria, it contains no mitochondrial translocation signal sequence. Northern blot analysis revealed that TK2 was ubiquitously expressed as 2 transcripts of 2.4 and 4 kb. Expression of the TK2 cDNA revealed a 60-kD protein with phosphorylation activity similar to purified human TK2. Based on the partial protein sequence of human TK2, Wang et al. (1999) isolated a human brain TK2 cDNA. These authors noted that although the cDNA they isolated corresponds to the full-length mature protein, it is likely to be incomplete because it lacks the coding region for a

mitochondrial target presequence. They reported that the predicted protein sequence matched that of purified TK2, but differed at the N-terminus and at amino acid 28 from the TK2 sequence deduced by Johansson and Karlsson (1997). TK2 shares approximately 40% identity with deoxycytidine kinase (OMIM Ref. No. 125450) and deoxyguanosine kinase (OMIM Ref. No. 601465) on the amino acid level. Wang et al. (1999) characterized both recombinant and native TK2 forms and found that the enzyme has broad substrate specificity and complex kinetics, suggesting that it may play a role in the activation of chemotherapeutic nucleoside analogs. Northern blot analysis indicated that the TK2 gene was expressed as multiple transcripts, some of which show a tissue-specific pattern. The highest levels of expression were observed in testis and ovary. Saada et al. (2001) identified 2 mutations in TK2, his90 to asn(188250.0001) and ile181 to asn(188250.0002), in 4 individuals who developed devastating myopathy and depletion of muscular mtDNA in infancy. In these individuals, the activity of TK2 in muscle mitochondria was reduced to 14 to 45% of the mean value in healthy control individuals. Mandel et al. (2001) identified mutations in the DGUOK gene in another form of

mtDNA depletion syndrome, the hepatocerebral form (see OMIM Ref. No. 251880). They noted that the main supply of dNTPs for mtDNA synthesis comes from the salvage pathway initiated by DGK and TK2. The association of mtDNA depletion with mutations in the genes encoding these 2 kinases suggested that the salvage pathway enzymes are involved in the maintenance of balanced mitochondrial dNTP pools.

[13440] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13441] Wang, L.; Munch-Petersen, B.; Herrstrom Sjoberg, A.; Hellman, U.; Bergman, T.; Jornvall, H.; Eriksson, S. : Human thymidine kinase 2: molecular cloning and characterisation of the enzyme activity with antiviral and cytostatic nucleoside substrates. FEBS Lett. 443: 170-174, 1999. ; and

[13442] Saada, A.; Shaag, A.; Mandel, H.; Nevo, Y.; Eriksson, S.; Elpeleg, O. : Mutant mitochondrial thymidine kinase in mitochondrial DNA depletion myopathy. Nature Genet. 29: 342-344, 2001.

[13443] Further studies establishing the function and utilities of TK2 are found in John Hopkins OMIM database record ID

188250, and in cited publications numbered 10085–10089 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. WAS Protein Family, Member 1 (WASF1, Accession NM_003931) is another VGAM210 host target gene. WASF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by WASF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WASF1 BINDING SITE, designated SEQ ID:10031, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13444] Another function of VGAM210 is therefore inhibition of WAS Protein Family, Member 1 (WASF1, Accession NM_003931), a gene which is a downstream effector molecules involved in the transmission of signals to the actin cytoskeleton. Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WASF1. The function of WASF1 has been established by previous studies. Eden et al. (2002) reported a mechanism by which RAC1 and the adaptor protein NCK (OMIM Ref. No. 600508) activate

actin nucleation through WAVE1. WAVE1 exists in a heterotetrameric complex that includes orthologs of human PIR121 (OMIM Ref. No. 606323), NAP125 (OMIM Ref. No. 604891), and HSPC300. Whereas recombinant WAVE1 is constitutively active, the WAVE1 complex is inactive. Eden et al. (2002) proposed that Rac1 and Nck cause dissociation of the WAVE1 complex, which releases active WAVE1-HSPC300 and leads to actin nucleation. Eden et al. (2002) also determined that ABI2 (OMIM Ref. No. 606442) interacts with WAVE1 and appears to remain associated with the NAP125-PIR121 subcomplex upon dissociation of the WAVE1 complex. By searching databases for WASP-like molecules containing the highly conserved verprolin homology (VPH) domain, Miki et al. (1998) identified the KIAA0269 cDNA (Nagase et al., 1996) encoding WASF1, which they called WAVE. Sequence analysis predicted that WASF1 has no similarity to WASP or WASL in the N terminus, through which WASP and WASL are regulated by CDC42. The N terminus of WASF1 contains a putative leucine zipper motif and a highly basic region. The midsequence proline-rich region and the C-terminal VPH domain and highly acidic region of WASF1 are similar to WASP family proteins. Western blot analysis showed

higher expression of WASF1 in neuronal cell lines than in fibroblast or kidney cell lines. Confocal microscopy demonstrated that WASF1 is expressed in a dot-like pattern in the cytoplasm and is concentrated in RAC-regulated membrane-ruffling areas. Mutational analysis and immunofluorescence microscopy showed that WASF1 induces actin reorganization downstream of RAC. By screening a brain cDNA library using a yeast 2-hybrid

[13445] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13446] Eden, S.; Rohatgi, R.; Podtelejnikov, A. V.; Mann, M.; Kirschner, M. W. : Mechanism of regulation of WAVE1-induced actin nucleation by Rac1 and Nck. Nature 418: 790–793, 2002. ; and

[13447] Nagase, T.; Seki, N.; Ishikawa, K.; Ohira, M.; Kawarabayashi, Y.; Ohara, O.; Tanaka, A.; Kotani, H.; Miyajima, N.; Nomura, N. : Prediction of the coding sequences of unidentified human gen.

[13448] Further studies establishing the function and utilities of WASF1 are found in John Hopkins OMIM database record ID 605035, and in cited publications numbered 10410, 1063 and 9011 listed in the bibliography section herein–

below, which are also hereby incorporated by reference. DKFZp434N074 (Accession XM_031481) is another VGAM210 host target gene. DKFZp434N074 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp434N074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434N074 BINDING SITE, designated SEQ ID:31389, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13449] Another function of VGAM210 is therefore inhibition of DKFZp434N074 (Accession XM_031481). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434N074. FLJ21477 (Accession NM_025153) is another VGAM210 host target gene. FLJ21477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21477 BINDING SITE, designated SEQ ID:24789, to the

nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13450] Another function of VGAM210 is therefore inhibition of FLJ21477 (Accession NM_025153). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21477. HSPC054 (Accession NM_014152) is another VGAM210 host target gene. HSPC054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC054 BINDING SITE, designated SEQ ID:15433, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13451] Another function of VGAM210 is therefore inhibition of HSPC054 (Accession NM_014152). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC054. P37NB (Accession NM_005824) is another VGAM210 host target gene. P37NB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by P37NB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P37NB BINDING SITE, designated SEQ ID:12434, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13452] Another function of VGAM210 is therefore inhibition of P37NB (Accession NM_005824). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P37NB. LOC114971 (Accession XM_054936) is another VGAM210 host target gene. LOC114971 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC114971 BINDING SITE, designated SEQ ID:36209, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13453] Another function of VGAM210 is therefore inhibition of LOC114971 (Accession XM_054936). Accordingly, utilities

of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114971. LOC133686 (Accession XM_059667) is another VGAM210 host target gene. LOC133686 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC133686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133686 BINDING SITE, designated SEQ ID:37056, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13454] Another function of VGAM210 is therefore inhibition of LOC133686 (Accession XM_059667). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133686. LOC146226 (Accession XM_096946) is another VGAM210 host target gene. LOC146226 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146226, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC146226 BINDING SITE, designated SEQ ID:40662, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13455] Another function of VGAM210 is therefore inhibition of LOC146226 (Accession XM_096946). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146226. LOC253263 (Accession XM_173102) is another VGAM210 host target gene. LOC253263 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253263 BINDING SITE, designated SEQ ID:46361, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13456] Another function of VGAM210 is therefore inhibition of LOC253263 (Accession XM_173102). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253263. LOC90362 (Accession XM_031163) is another VGAM210 host target gene. LOC90362 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90362 BINDING SITE, designated SEQ ID:31295, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13457] Another function of VGAM210 is therefore inhibition of LOC90362 (Accession XM_031163). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90362. LOC91263 (Accession XM_037264) is another VGAM210 host target gene. LOC91263 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91263, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91263 BINDING SITE, designated SEQ ID:32596, to the nucleotide sequence of VGAM210 RNA, herein designated VGAM RNA, also designated SEQ ID:2921.

[13458] Another function of VGAM210 is therefore inhibition of

LOC91263 (Accession XM_037264). Accordingly, utilities of VGAM210 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91263. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 211 (VGAM211) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13459] VGAM211 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM211 was detected is described hereinabove with reference to Figs. 1–8.

[13460] VGAM211 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian Virus 40.

VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13461] VGAM211 gene encodes a VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM211 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM211 precursor RNA is designated SEQ ID:197, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:197 is located at position 112 relative to the genome of Simian Virus 40.

[13462] VGAM211 precursor RNA folds onto itself, forming VGAM211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13463] An enzyme complex designated DICER COMPLEX, `dices` the VGAM211 folded precursor RNA into VGAM211 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide se-

quence of VGAM211 RNA is designated SEQ ID:2922, and is provided hereinbelow with reference to the sequence listing part.

[13464] VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM211 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[13465] VGAM211 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM211 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM211 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[13466] The complementary binding of VGAM211 RNA, herein designated VGAM RNA, to host target binding sites on VGAM211 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM211 host target RNA into VGAM211 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13467] It is appreciated that VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM211 host target genes. The mRNA of each one of this plurality of VGAM211 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM211 RNA, herein designated VGAM RNA, and which when bound by VGAM211 RNA causes inhibition of translation of respective one or more VGAM211 host target proteins.

[13468] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM211 gene, herein designated VGAM GENE, on one or more VGAM211 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13469] It is yet further appreciated that a function of VGAM211 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of viral infection by Simian Virus 40. Specific functions, and accordingly utilities, of VGAM211 correlate with, and may be deduced from, the identity of the host target genes which VGAM211 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13470] Nucleotide sequences of the VGAM211 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM211 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM211 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM211 are further described hereinbelow with reference to Table 1.

[13471] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM211 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM211 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13472] As mentioned hereinabove with reference to Fig. 1, a function of VGAM211 gene, herein designated VGAM is inhibition of expression of VGAM211 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM211 correlate with, and may be deduced from, the identity of the target genes which VGAM211 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13473] A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 3 (ADAMTS3, Accession NM_014243) is a VGAM211 host target gene. ADAMTS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADAMTS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAMTS3 BINDING SITE, designated SEQ ID:15509, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13474] A function of VGAM211 is therefore inhibition of A Disintegrin-like and Metalloprotease (reprolysin type) with Thrombospondin Type 1 Motif, 3 (ADAMTS3, Accession

NM_014243), a gene which cleaves the propeptides of type ii collagen prior to fibril assembly. Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAMTS3. The function of ADAMTS3 has been established by previous studies. Members of the ADAMTS family contain a signal peptide, a prodomain, a metalloproteinase domain, a disintegrin-like domain, varying numbers of thrombospondin type 1 motifs, and a cysteine-rich domain. See ADAMTS5 (OMIM Ref. No. 605007) for additional background information on the ADAMTS family. By sequencing randomly selected cDNAs corresponding to relatively long transcripts from human brain, Nagase et al. (1997) identified a partial ADAMTS3 cDNA, which they called KIAA0366, that lacked 5-prime coding sequence. The deduced partial ADAMTS3 protein had 1,201 amino acids. In vitro transcribed/translated ADAMTS3 protein had an apparent molecular mass of larger than 100 kD by SDS-PAGE. The authors examined ADAMTS3 expression in 14 human tissues using RT-PCR. By radiation hybrid mapping, Nagase et al. (1997) mapped the ADAMTS3 gene to chromosome 4. Hurskainen et al. (1999) mapped the ADAMTS3 gene to chromosome 4 using somatic cell hy-

brid analysis. They localized the ADAMTS3 gene to 4q21 by radiation hybrid mapping.

[13475] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13476] Nagase, T.; Ishikawa, K.; Nakajima, D.; Ohira, M.; Seki, N.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 4: 141–150, 1997. ; and

[13477] Hurskainen, T. L.; Hirohata, S.; Seldin, M. F.; Apte, S. S. : ADAM–TS5, ADAM–TS6, and ADAM–TS7, novel members of a new family of zinc metalloproteases: general features and genomic distr.

[13478] Further studies establishing the function and utilities of ADAMTS3 are found in John Hopkins OMIM database record ID 605011, and in cited publications numbered 760 and 7605 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ADP–ribosylation Factor 4–like (ARF4L, Accession XM_045890) is another VGAM211 host target gene. ARF4L BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by ARF4L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF4L BINDING SITE, designated SEQ ID:34604, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13479] Another function of VGAM211 is therefore inhibition of ADP-ribosylation Factor 4-like (ARF4L, Accession XM_045890). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARF4L. ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B) (ELAVL2, Accession NM_004432) is another VGAM211 host target gene. ELAVL2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ELAVL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELAVL2 BINDING SITE, designated SEQ ID:10717, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13480] Another function of VGAM211 is therefore inhibition of ELAV (embryonic lethal, abnormal vision, *Drosophila*)-like 2 (Hu antigen B) (ELAVL2, Accession NM_004432), a gene which binds rna. seems to recognize a gaaa motif. can bind to its own 3' untranslated region (3'utr), the c-fos 3'utr and the id 3'utr. Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELAVL2. The function of ELAVL2 has been established by previous studies. Hel-N1 is an evolutionarily conserved neural-specific RNA-binding protein expressed in neurons of the brain. The rat and human cDNAs were cloned by King et al. (1994). The human cDNA, symbolized ELAVL2 for 'embryonic lethal abnormal vision-like 2,' encodes a predicted 359-amino acid protein that shows significant similarity to the product of the *Drosophila* elav gene, the absence of which causes multiple structural defects and hypotrophy of the fly's central nervous system. In situ hybridization of rat tissues demonstrated that the mRNA occurs within a subset of neurons of the hippocampus, cortex, and other areas of the gray matter (King et al., 1994). Hel-N1 was shown to bind in vitro to the 3-prime untranslated region of an mRNA for Id (OMIM Ref. No. 600349), an inhibitor of

DNA binding. King (1994) showed that alternative splicing of a 91-bp exon produces a longer isoform. The ELAVL2-homologous gene is referred to as Hub in the mouse. It is one of the tumor antigens that underlie paraneoplastic neurologic disorders (PND), which arise when an immune response to systemic tumors expressing neuronal proteins ('onconeural antigens') develops into an autoimmune neuronal degeneration (Fletcher et al., 1997). It is in the class of neuron-specific RNA-binding proteins. Han et al. (1996) mapped the ELAVL2 gene to 9p21 by chromosome microdissection PCR and by fluorescence in situ hybridization. Fletcher et al. (1997) demonstrated that the mouse gene maps to mouse chromosome 4 close to the homolog of interferon alpha (OMIM Ref. No. 147660), which maps to 9p22 in the human genome

[13481] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13482] Fletcher, C. F.; Okano, H. J.; Gilbert, D. J.; Yang, Y.; Yang, C.; Copeland, N. G.; Jenkins, N. A.; Darnell, R. B. : Mouse chromosomal locations of nine genes encoding homologs of human paraneoplastic neurologic disorder antigens. Genomics 45: 313–319, 1997. ; and

[13483] Han, J.; Knops, J. F.; Longshore, J. W.; King, P. H. : Localization of human elav-like neuronal protein 1 (Hel-N1) on chromosome 9p21 by chromosome microdissection polymerase chain react.

[13484] Further studies establishing the function and utilities of ELAVL2 are found in John Hopkins OMIM database record ID 601673, and in cited publications numbered 238 and 9482-9484 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fyn-related Kinase (FRK, Accession NM_002031) is another VGAM211 host target gene. FRK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FRK BINDING SITE, designated SEQ ID:7785, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13485] Another function of VGAM211 is therefore inhibition of Fyn-related Kinase (FRK, Accession NM_002031), a gene which binds pRb (RB1) during G1 and S phase and suppresses growth. Accordingly, utilities of VGAM211 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with FRK. The function of FRK and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM157. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184) is another VGAM211 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31302, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13486] Another function of VGAM211 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1. Transcription Elongation Factor A (SII), 1 (TCEA1, Accession XM_087370) is another VGAM211 host target gene.

TCEA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCEA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCEA1 BINDING SITE, designated SEQ ID:39202, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13487] Another function of VGAM211 is therefore inhibition of Transcription Elongation Factor A (SII), 1 (TCEA1, Accession XM_087370), a gene which helps RNA polymerase II to transcribe past blockages. Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCEA1. The function of TCEA1 has been established by previous studies. Transcription elongation factors help RNA polymerase II (see OMIM Ref. No. 180660) to transcribe past blockages due to specific DNA sequences, DNA-binding proteins, and transcription-arresting drugs. Transcription elongation factors in humans fall into 2 classes: the SIII (see OMIM Ref. No. 600788)/TF2F (see OMIM Ref. No. 189968) class, members of which increase the average

rate of RNA chain elongation (Aso et al., 1995); and the SII class, which releases RNA polymerase II from transcriptional arrest (Reines, 1994). Park et al. (1994) cloned and characterized a human gene encoding an SII-type elongation factor. The gene, designated TFIIIS by them, is 2.8 kb long, intronless, and produces a 2.5-kb transcript. DiMarco et al. (1996) designed PCR primers for the SII gene (also symbolized TCEA) and mapped it to human chromosome 3 by analysis of human-rodent hybrid mapping panel. Further regionalization to 3p22-p21.3 was accomplished by fluorescence in situ hybridization using a YAC containing the gene. DiMarco et al. (1996) cited reports that this region of 3p exhibits loss of heterozygosity (LOH) in small- and non-small-cell lung carcinomas as well as several other malignancies. Thomas et al. (1998) addressed whether the intrinsic 3-prime to 5-prime nuclease activity of human RNA polymerase II (OMIM Ref. No. pol II) can proofread during transcription in vitro. In the presence of SII, a protein that stimulates the nuclease activity, pol II quantitatively removed misincorporated nucleotides from the nascent transcript during rapid chain extension. The basis of discrimination between the correct and incorrect base was the slow addition of the next nu-

cleotide to the mismatched terminus. Incorporation of inosine monophosphate inhibited the next nucleotide addition by a similar magnitude as a mismatched base.

Thomas et al. (1998) demonstrated that addition of SII to a transcription reaction dramatically altered the RNA base content, reflecting the stable incorporation of more 'correct' (GMP) and fewer 'incorrect' (IMP) nucleotides.

[13488] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13489] DiMarco, S. P.; Glover, T. W.; Miller, D. E.; Reines, D.; Warren, S. T. : Transcription elongation factor SII (TCEA) maps to human chromosome 3p22–p21.3. *Genomics* 36: 185–188, 1996. ; and

[13490] Thomas, M. J.; Platas, A. A.; Hawley, D. K. : Transcriptional fidelity and proofreading by RNA polymerase II. *Cell* 93: 627–637, 1998.

[13491] Further studies establishing the function and utilities of TCEA1 are found in John Hopkins OMIM database record ID 601425, and in cited publications numbered 1020 and 9273–9276 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 5 Open Reading Frame 4 (C5orf4, Ac-

cession NM_016348) is another VGAM211 host target gene. C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by C5orf4, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C5orf4 BINDING SITE1 and C5orf4 BINDING SITE2, designated SEQ ID:18474 and SEQ ID:26180 respectively, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13492] Another function of VGAM211 is therefore inhibition of Chromosome 5 Open Reading Frame 4 (C5orf4, Accession NM_016348). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C5orf4. FLJ11175 (Accession NM_018349) is another VGAM211 host target gene. FLJ11175 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11175, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11175 BINDING SITE, designated

SEQ ID:20360, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13493] Another function of VGAM211 is therefore inhibition of FLJ11175 (Accession NM_018349). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11175. FLJ14054 (Accession NM_024563) is another VGAM211 host target gene. FLJ14054 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14054 BINDING SITE, designated SEQ ID:23785, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13494] Another function of VGAM211 is therefore inhibition of FLJ14054 (Accession NM_024563). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14054. Hippocalcin Like 4 (HPCAL4, Accession NM_016257) is another VGAM211 host target gene. HPCAL4 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPCAL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HPCAL4 BINDING SITE, designated SEQ ID:18387, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13495] Another function of VGAM211 is therefore inhibition of Hippocalcin Like 4 (HPCAL4, Accession NM_016257). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPCAL4. KIAA0931 (Accession XM_041191) is another VGAM211 host target gene. KIAA0931 BINDING SITE1 and KIAA0931 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by KIAA0931, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0931 BINDING SITE1 and KIAA0931 BINDING SITE2, designated SEQ ID:33483 and SEQ ID:33485 respectively, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA,

also designated SEQ ID:2922.

[13496] Another function of VGAM211 is therefore inhibition of KIAA0931 (Accession XM_041191). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0931. KIAA1198 (Accession XM_032674) is another VGAM211 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31709, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13497] Another function of VGAM211 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. PXR2b (Accession NM_016559) is another VGAM211 host target gene. PXR2b BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PXR2b, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PXR2b BINDING SITE, designated SEQ ID:18633, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13498] Another function of VGAM211 is therefore inhibition of PXR2b (Accession NM_016559). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PXR2b. LOC120856 (Accession XM_058509) is another VGAM211 host target gene. LOC120856 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC120856, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC120856 BINDING SITE, designated SEQ ID:36632, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13499] Another function of VGAM211 is therefore inhibition of LOC120856 (Accession XM_058509). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC120856. LOC200853 (Accession XM_114308) is another VGAM211 host target gene. LOC200853 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200853 BINDING SITE, designated SEQ ID:42866, to the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13500] Another function of VGAM211 is therefore inhibition of LOC200853 (Accession XM_114308). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200853. LOC203084 (Accession XM_113540) is another VGAM211 host target gene. LOC203084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203084 BINDING SITE, designated SEQ ID:42280, to

the nucleotide sequence of VGAM211 RNA, herein designated VGAM RNA, also designated SEQ ID:2922.

[13501] Another function of VGAM211 is therefore inhibition of LOC203084 (Accession XM_113540). Accordingly, utilities of VGAM211 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203084. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 212 (VGAM212) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13502] VGAM212 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM212 was detected is described hereinabove with reference to Figs. 1–8.

[13503] VGAM212 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian Virus 40. VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13504] VGAM212 gene encodes a VGAM212 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM212 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM212 precursor RNA is designated SEQ ID:198, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:198 is located at position 2253 relative to the genome of Simian Virus 40.

[13505] VGAM212 precursor RNA folds onto itself, forming VGAM212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13506] An enzyme complex designated DICER COMPLEX, `dices` the VGAM212 folded precursor RNA into VGAM212 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM212 RNA is designated SEQ ID:2923, and is provided hereinbelow with reference to the sequence listing part.

[13507] VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM212 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[13508] VGAM212 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM212 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM212 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13509] The complementary binding of VGAM212 RNA, herein designated VGAM RNA, to host target binding sites on VGAM212 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM212 host target RNA into VGAM212 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13510] It is appreciated that VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM212 host target genes. The mRNA of each one of this plurality of VGAM212 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM212 RNA, herein designated VGAM RNA, and which when bound by VGAM212 RNA causes inhibition of translation of respective one or more VGAM212 host target proteins.

[13511] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM212 gene, herein designated VGAM GENE, on one or more VGAM212 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[13512] It is yet further appreciated that a function of VGAM212 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of viral infection by Simian Virus 40. Specific functions, and accordingly utilities, of VGAM212 correlate with, and may be deduced from, the identity of the host target genes which VGAM212 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[13513] Nucleotide sequences of the VGAM212 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM212 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM212 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM212 are further described hereinbelow with reference to Table 1.

[13514] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM212 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM212 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13515] As mentioned hereinabove with reference to Fig. 1, a function of VGAM212 gene, herein designated VGAM is inhibition of expression of VGAM212 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM212 correlate with, and may be deduced from, the identity of the target genes which VGAM212 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13516] Acid Phosphatase 2, Lysosomal (ACP2, Accession NM_001610) is a VGAM212 host target gene. ACP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACP2 BINDING SITE, designated SEQ ID:7319, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13517] A function of VGAM212 is therefore inhibition of Acid Phosphatase 2, Lysosomal (ACP2, Accession NM_001610).

Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACP2. Angiopoietin 2 (ANGPT2, Accession NM_001147) is another VGAM212 host target gene.

ANGPT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ANGPT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANGPT2 BINDING SITE, designated SEQ ID:6818, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13518] Another function of VGAM212 is therefore inhibition of Angiopoietin 2 (ANGPT2, Accession NM_001147), a gene which is a vascular endothelial growth factor that acts as an antagonist of TIE2 (TEK) receptor protein tyrosine kinase. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANGPT2. The function of ANGPT2 has been established by previous studies. Tanaka et al. (1999) investigated angiopoietin expression in 23 samples of hepatocellular carcinoma (HCC) and paired adjacent

uninvolved liver samples to determine if these genes have a potential role in the growth and spread of the malignancy. They obtained the full coding sequence of a variant angiopoietin-2 cDNA from HCC specimens, and the biologic consequences of overexpression on tumor formation and hemorrhage were determined in an animal model system. Angiopoietin-1 was equally expressed in HCC and adjacent noncarcinomatous liver tissue. On the other hand, angiopoietin-2 was found to be highly expressed only in tumor tissue. In addition, angiopoietin-2 was expressed in 10 of 12 hypervascular HCCs, but only in 2 of 11 hypovascular HCCs. Ectopic expression of angiopoietin-2 in nonexpressing HCC cells promoted the rapid development of human hepatomas and produced hemorrhage within tumors in nude mice. These results suggested a role for angiopoietin-2 in the neovascularization of HCC. The enhanced gene expression may contribute to the clinical hypervascular phenotype as well as to tumor formation and progression. To explore the possibility that VEGF and angiopoietins collaborate during tumor angiogenesis, Holash et al. (1999) analyzed several different murine and human tumor models. Holash et al. (1999) noted that angiopoietin-1 was antiapoptotic for cultured

endothelial cells and expression of its antagonist angiopoietin-2 was induced in the endothelium of co-opted tumor vessels before their regression. Expression of Ang2 continued to mark not only the few surviving internal vessels but also the angiogenic vessels at the tumor margin, suggesting that the destabilizing action of angiopoietin-2 facilitates the angiogenic action of VEGF at the tumor rim. Holash et al. (1999) examined human glioblastomas. Angiopoietin-2 was not detectable in the normal human brain, but its expression was dramatically induced in co-opted tumor vessels, preceding vessel regression. Holash et al. (1999) implanted rat RBA mammary adenocarcinoma cells into rat brains. Co-opted vessels displayed striking and specific upregulation of angiopoietin-2, which was not detectable in the vessels of adjacent brain tissue. Holash et al. (1999) concluded that their observations indicate that a subset of tumors rapidly co-opts existing host vessels to form an initially well-vascularized tumor mass. Perhaps as part of a host defense mechanism there is widespread regression of these initially co-opted vessels, leading to a secondarily avascular tumor and a massive tumor cell loss. However, the remaining tumor is ultimately rescued by robust angiogenesis at the tumor mar-

gin.

- [13519] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [13520] Holash, J.; Maisonpierre, P. C.; Compton, D.; Boland, P.; Alexander, C. R.; Zagzag, D.; Yancopoulos, G. D.; Wiegand, S. J. : Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF. Science 284: 1994–1998, 1999. ; and
- [13521] Tanaka, S.; Mori, M.; Sakamoto, Y.; Makuuchi, M.; Sugimachi, K.; Wands, J. R. : Biologic significance of angiopoietin-2 expression in human hepatocellular carcinoma. J. Clin. Invest. 10.
- [13522] Further studies establishing the function and utilities of ANGPT2 are found in John Hopkins OMIM database record ID 601922, and in cited publications numbered 9394, 10441–581 and 9401 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Collagen, Type V, Alpha 3 (COL5A3, Accession NM_015719) is another VGAM212 host target gene. COL5A3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by COL5A3, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL5A3 BINDING SITE, designated SEQ ID:17934, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13523] Another function of VGAM212 is therefore inhibition of Collagen, Type V, Alpha 3 (COL5A3, Accession NM_015719). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL5A3. Deleted In Lymphocytic Leukemia, 2 (DLEU2, Accession NM_006021) is another VGAM212 host target gene. DLEU2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DLEU2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DLEU2 BINDING SITE, designated SEQ ID:12639, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13524] Another function of VGAM212 is therefore inhibition of Deleted In Lymphocytic Leukemia, 2 (DLEU2, Accession

NM_006021). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DLEU2. Junctional Adhesion Molecule 3 (JAM3, Accession NM_032801) is another VGAM212 host target gene. JAM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JAM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JAM3 BINDING SITE, designated SEQ ID:26556, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13525] Another function of VGAM212 is therefore inhibition of Junctional Adhesion Molecule 3 (JAM3, Accession NM_032801), a gene which is a member of the junctional adhesion molecule protein family. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JAM3. The function of JAM3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.V-myc Myelocytomatosis Viral Oncogene Ho-

molog 2 (avian) (MYCL2, Accession NM_005377) is another VGAM212 host target gene. MYCL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYCL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYCL2 BINDING SITE, designated SEQ ID:11859, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13526] Another function of VGAM212 is therefore inhibition of V-myc Myelocytomatosis Viral Oncogene Homolog 2 (avian) (MYCL2, Accession NM_005377). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYCL2. Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507) is another VGAM212 host target gene. NGFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFR BINDING SITE, desig-

nated SEQ ID:8337, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13527] Another function of VGAM212 is therefore inhibition of Nerve Growth Factor Receptor (TNFR superfamily, member 16) (NGFR, Accession NM_002507), a gene which can mediate cell survival as well as cell death of neural cells. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFR. The function of NGFR has been established by previous studies. Bothwell (1996), Carter and Lewin (1997), and Bibel and Barde (2000) reviewed neurotrophins and their receptors. Nerve growth factor receptor (NGFR) is also referred to as p75(NTR) due to its molecular mass and its ability to bind at low affinity not only NGF (see OMIM Ref. No. 162030), but also other neurotrophins, including brain-derived neurotrophic factor (BDNF; 113505), neurotrophin-3 (NTF3; 162660), and neurotrophin-4/5 (NTF5; 162662). At the time of its discovery, NGFR was considered a unique type of protein. Subsequently, however, a large superfamily of tumor necrosis factor receptors were found to share the overall structure of NGFR (4 extracellular ligand-binding, cys-

teine-rich repeats, or CRs, and signaling through association with, or disassociation from, cytoplasmic interactors). The identification of this superfamily helped elucidate some of the biologic functions of NGFR, including its ultimate involvement in the nuclear factor kappa-B (NFKB; OMIM Ref. No. 164011) and apoptosis pathways. As a monomer, NGFR binds NGF with low affinity. Higher affinity binding is achieved by association with higher molecular mass, low-affinity neurotrophin receptors, namely the tropomyosin receptor kinases, TRKA (NTRK1; 191315), TRKB (NTRK2; 600456), and TRKC (NTRK3; 191316). TRKA, TRKB, and TRKC are specific for or 'preferred by' NGF, NTF5 and BDNF, and NTF3, respectively (Ip et al., 1993). NTF3 also binds to TRKA and TRKB, but with significantly lower affinity. Animal model experiments lend further support to the function of NGFR. By targeted disruption of exon 3 of the *Ngfr* gene, which encodes CR2, CR3, and CR4, Lee et al. (1992) generated mice lacking functional *Ngfr*. The *Ngfr* $-/-$ mice were viable and fertile but developed skin defects in all extremities as well as ulcers that were prone to secondary infection with loss of epidermis. Immunohistochemistry revealed a lack of calcitonin gene-related peptide (CALCA; 114130)- and sub-

stance P (OMIM Ref. No. 162320)–expressing peripheral sensory nerve fibers. Mutant mice had a loss of heat sensitivity but no defects in innervation of the iris or salivary gland. Mice carrying a single copy of a human NGFR transgene did not have neuropeptide and sensory loss or the peripheral ulcers.

[13528] It is appreciated that the abovementioned animal model for NGFR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13529] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13530] Bibel, M.; Barde, Y.–A. : Neurotrophins: key regulators of cell fate and cell shape in the vertebrate nervous system. *Genes Dev.* 14: 2919–2937, 2000. ; and

[13531] Lee, K. F.; Li, E.; Huber, J.; Landis, S. C.; Sharpe, A. H.; Chao, M. V.; Jaenisch, R. : Targeted mutation of the gene encoding the low affinity NGF receptor p75 leads to deficits in t.

[13532] Further studies establishing the function and utilities of NGFR are found in John Hopkins OMIM database record ID 162010, and in cited publications numbered 1938–1944,

181 and 2227-2235 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM_001334) is another VGAM212 host target gene. POU3F1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POU3F1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POU3F1 BINDING SITE, designated SEQ ID:29832, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13533] Another function of VGAM212 is therefore inhibition of POU Domain, Class 3, Transcription Factor 1 (POU3F1, Accession XM_001334), a gene which involves in early embryogenesis and neurogenesis. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POU3F1. The function of POU3F1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM85. Selenoprotein N, 1 (SEPN1, Accession

XM_039033) is another VGAM212 host target gene. SEPN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPN1 BINDING SITE, designated SEQ ID:32990, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13534] Another function of VGAM212 is therefore inhibition of Selenoprotein N, 1 (SEPN1, Accession XM_039033). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEPN1. Vesicle Amine Transport Protein 1 Homolog (T californica) (VAT1, Accession NM_006373) is another VGAM212 host target gene. VAT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VAT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAT1 BINDING SITE, designated SEQ ID:13068, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA,

also designated SEQ ID:2923.

[13535] Another function of VGAM212 is therefore inhibition of Vesicle Amine Transport Protein 1 Homolog (T californica) (VAT1, Accession NM_006373), a gene which is a membrane protein of cholinergic synaptic vesicles. Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAT1. The function of VAT1 has been established by previous studies. Synaptic vesicles are responsible for regulating the storage and release of neurotransmitters in the nerve terminal. Using expression screening of a marine ray (Torpedo) electric lobe library, Linial et al. (1989) identified a cDNA encoding a 379-amino acid synaptic vesicle integral membrane protein, which they termed VAT1. Northern blot analysis revealed that a 5.8-kb transcript is expressed in electromotor neurons. Western blot analysis determined expression of a 42-kD protein in the electric organ that copurified with synaptic vesicles. While attempting to identify the BRCA1 (OMIM Ref. No. 113705) gene, Friedman et al. (1995) cloned cDNAs for a number of genes on chromosome 17q21, including one with significant homology to Torpedo VAT1. By random sequencing of 4 cosmids from a human chro-

mosome 17-specific library, Smith et al. (1996) identified the sequence of 2 complete genes within 117 kb of DNA containing the BRCA1 gene: RHO7 (OMIM Ref. No. 601555) and VAT1, an abundant membrane protein of cholinergic synaptic vesicles. The coding sequence of VAT1 predicts a 301-amino acid peptide. The authors found that a CpG island precedes the VAT1 gene, which contains 6 exons spanning 8.1 kb. They determined the following order of genes in this region: cen--IFP35 (OMIM Ref. No. 600735)--VAT1--RHO7--BRCA1--1A1-3B--tel.

[13536] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13537] Linial, M.; Miller, K.; Scheller, R. H. : VAT-1: an abundant membrane protein from Torpedo cholinergic synaptic vesicles. Neuron 2: 1265-1273, 1989. ; and

[13538] Friedman, L. S.; Ostermeyer, E. A.; Lynch, E. D.; Welcsh, P.; Szabo, C. I.; Meza, J. E.; Anderson, L. A.; Dowd, P.; Lee, M. K.; Rowell, S. E.; Ellison, J.; Boyd, J.; King, M.-C. : 22 genes.

[13539] Further studies establishing the function and utilities of VAT1 are found in John Hopkins OMIM database record ID 604631, and in cited publications numbered 4982-4984

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Bromodomain and PHD Finger Containing, 3 (BRPF3, Accession XM_166450) is another VGAM212 host target gene. BRPF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRPF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRPF3 BINDING SITE, designated SEQ ID:44345, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13540] Another function of VGAM212 is therefore inhibition of Bromodomain and PHD Finger Containing, 3 (BRPF3, Accession XM_166450). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BRPF3. DKFZP434P0721 (Accession XM_033181) is another VGAM212 host target gene. DKFZP434P0721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZP434P0721 BINDING SITE, designated SEQ ID:31871, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13541] Another function of VGAM212 is therefore inhibition of DKFZP434P0721 (Accession XM_033181). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0721. Family with Sequence Similarity 3, Member D (FAM3D, Accession NM_138805) is another VGAM212 host target gene. FAM3D BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FAM3D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAM3D BINDING SITE, designated SEQ ID:29029, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13542] Another function of VGAM212 is therefore inhibition of Family with Sequence Similarity 3, Member D (FAM3D, Accession NM_138805). Accordingly, utilities of VGAM212

include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAM3D. FHX (Accession NM_018416) is another VGAM212 host target gene. FHX BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FHX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FHX BINDING SITE, designated SEQ ID:20464, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13543] Another function of VGAM212 is therefore inhibition of FHX (Accession NM_018416). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FHX. FLJ12800 (Accession NM_022903) is another VGAM212 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800 BINDING SITE, designated SEQ ID:23195, to the nucleotide sequence of

VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13544] Another function of VGAM212 is therefore inhibition of FLJ12800 (Accession NM_022903). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ13955 (Accession NM_024759) is another VGAM212 host target gene. FLJ13955 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13955 BINDING SITE, designated SEQ ID:24110, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13545] Another function of VGAM212 is therefore inhibition of FLJ13955 (Accession NM_024759). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13955. FLJ20666 (Accession NM_017922) is another VGAM212 host target gene. FLJ20666 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ20666, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20666 BINDING SITE, designated SEQ ID:19587, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13546] Another function of VGAM212 is therefore inhibition of FLJ20666 (Accession NM_017922). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20666. FLJ20958 (Accession NM_022102) is another VGAM212 host target gene. FLJ20958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20958 BINDING SITE, designated SEQ ID:22647, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13547] Another function of VGAM212 is therefore inhibition of FLJ20958 (Accession NM_022102). Accordingly, utilities of

VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20958. G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_139201) is another VGAM212 host target gene. GIT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GIT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE, designated SEQ ID:29214, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13548] Another function of VGAM212 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_139201). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. HPIP (Accession NM_020524) is another VGAM212 host target gene. HPIP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HPIP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of HPIP BINDING SITE, designated SEQ ID:21739, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13549] Another function of VGAM212 is therefore inhibition of HPIP (Accession NM_020524). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HPIP. KIAA0544 (Accession XM_048119) is another VGAM212 host target gene. KIAA0544 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0544, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0544 BINDING SITE, designated SEQ ID:35114, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13550] Another function of VGAM212 is therefore inhibition of KIAA0544 (Accession XM_048119). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0544. KIAA1198 (Accession XM_032674) is another VGAM212 host target gene. KIAA1198 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31711, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13551] Another function of VGAM212 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. MGC12538 (Accession NM_032746) is another VGAM212 host target gene. MGC12538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12538 BINDING SITE, designated SEQ ID:26483, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13552] Another function of VGAM212 is therefore inhibition of

MGC12538 (Accession NM_032746). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12538. MGC15854 (Accession NM_145029) is another VGAM212 host target gene. MGC15854 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC15854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15854 BINDING SITE, designated SEQ ID:29645, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13553] Another function of VGAM212 is therefore inhibition of MGC15854 (Accession NM_145029). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15854. MGC2541 (Accession NM_080670) is another VGAM212 host target gene. MGC2541 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2541, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC2541 BINDING SITE, designated SEQ ID:27966, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13554] Another function of VGAM212 is therefore inhibition of MGC2541 (Accession NM_080670). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2541. MGC4707 (Accession NM_024113) is another VGAM212 host target gene. MGC4707 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4707, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4707 BINDING SITE, designated SEQ ID:23563, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13555] Another function of VGAM212 is therefore inhibition of MGC4707 (Accession NM_024113). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4707. Polymerase (DNA directed), Mu (POLM, Acces-

sion XM_165867) is another VGAM212 host target gene. POLM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by POLM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of POLM BINDING SITE, designated SEQ ID:43786, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13556] Another function of VGAM212 is therefore inhibition of Polymerase (DNA directed), Mu (POLM, Accession XM_165867). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with POLM. Scavenger Receptor Cysteine Rich Domain Containing, Group B (4 domains) (SRCRB4D, Accession NM_080744) is another VGAM212 host target gene. SRCRB4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SRCRB4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SRCRB4D BINDING SITE, designated SEQ ID:28031, to the nucleotide sequence of

VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13557] Another function of VGAM212 is therefore inhibition of Scavenger Receptor Cysteine Rich Domain Containing, Group B (4 domains) (SRCRB4D, Accession NM_080744). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SRCRB4D. LOC126669 (Accession XM_060121) is another VGAM212 host target gene. LOC126669 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC126669, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC126669 BINDING SITE, designated SEQ ID:37160, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13558] Another function of VGAM212 is therefore inhibition of LOC126669 (Accession XM_060121). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC126669. LOC131000 (Accession XM_067145) is an-

other VGAM212 host target gene. LOC131000 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131000, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131000 BINDING SITE, designated SEQ ID:37349, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13559] Another function of VGAM212 is therefore inhibition of LOC131000 (Accession XM_067145). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131000. LOC147639 (Accession XM_085822) is another VGAM212 host target gene. LOC147639 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147639, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147639 BINDING SITE, designated SEQ ID:38346, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13560] Another function of VGAM212 is therefore inhibition of LOC147639 (Accession XM_085822). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147639. LOC148189 (Accession XM_086087) is another VGAM212 host target gene. LOC148189 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148189 BINDING SITE, designated SEQ ID:38487, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13561] Another function of VGAM212 is therefore inhibition of LOC148189 (Accession XM_086087). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148189. LOC151124 (Accession XM_098006) is another VGAM212 host target gene. LOC151124 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151124, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151124 BINDING SITE, designated SEQ ID:41301, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13562] Another function of VGAM212 is therefore inhibition of LOC151124 (Accession XM_098006). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151124. LOC157381 (Accession XM_098754) is another VGAM212 host target gene. LOC157381 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157381, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157381 BINDING SITE, designated SEQ ID:41789, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13563] Another function of VGAM212 is therefore inhibition of LOC157381 (Accession XM_098754). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC157381. LOC158450 (Accession XM_088580) is another VGAM212 host target gene. LOC158450 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158450 BINDING SITE, designated SEQ ID:39842, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13564] Another function of VGAM212 is therefore inhibition of LOC158450 (Accession XM_088580). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158450. LOC158504 (Accession XM_088591) is another VGAM212 host target gene. LOC158504 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158504 BINDING SITE, designated SEQ ID:39853, to the nucleotide sequence of VGAM212 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2923.

[13565] Another function of VGAM212 is therefore inhibition of LOC158504 (Accession XM_088591). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158504. LOC199923 (Accession XM_114057) is another VGAM212 host target gene. LOC199923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199923 BINDING SITE, designated SEQ ID:42668, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13566] Another function of VGAM212 is therefore inhibition of LOC199923 (Accession XM_114057). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199923. LOC90246 (Accession XM_030283) is another VGAM212 host target gene. LOC90246 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90246, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90246 BINDING SITE, designated SEQ ID:31004, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13567] Another function of VGAM212 is therefore inhibition of LOC90246 (Accession XM_030283). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90246. LOC91450 (Accession XM_038515) is another VGAM212 host target gene. LOC91450 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC91450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91450 BINDING SITE, designated SEQ ID:32855, to the nucleotide sequence of VGAM212 RNA, herein designated VGAM RNA, also designated SEQ ID:2923.

[13568] Another function of VGAM212 is therefore inhibition of LOC91450 (Accession XM_038515). Accordingly, utilities of VGAM212 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC91450. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 213 (VGAM213) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13569] VGAM213 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM213 was detected is described hereinabove with reference to Figs. 1–8.

[13570] VGAM213 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Simian Virus 40. VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13571] VGAM213 gene encodes a VGAM213 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM213 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM213 precursor RNA is designated SEQ

ID:199, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:199 is located at position 4571 relative to the genome of Simian Virus 40.

[13572] VGAM213 precursor RNA folds onto itself, forming VGAM213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13573] An enzyme complex designated DICER COMPLEX, `dices` the VGAM213 folded precursor RNA into VGAM213 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 88%) nucleotide sequence of VGAM213 RNA is designated SEQ ID:2924, and is provided hereinbelow with reference to the sequence

listing part.

[13574] VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM213 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13575] VGAM213 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM213 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM213 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13576] The complementary binding of VGAM213 RNA, herein designated VGAM RNA, to host target binding sites on VGAM213 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM213 host target RNA into VGAM213 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13577] It is appreciated that VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM213 host target genes. The mRNA of each one of this plurality of VGAM213 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM213 RNA, herein designated VGAM

RNA, and which when bound by VGAM213 RNA causes inhibition of translation of respective one or more VGAM213 host target proteins.

[13578] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM213 gene, herein designated VGAM GENE, on one or more VGAM213 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13579] It is yet further appreciated that a function of VGAM213 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM213 include diagnosis, prevention and treatment of viral infection by Simian Virus 40. Specific functions, and accordingly utilities, of VGAM213 correlate with, and may be deduced from, the identity of the host target genes which VGAM213 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13580] Nucleotide sequences of the VGAM213 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM213 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM213 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM213 are further described hereinbelow with reference to Table 1.

[13581] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM213 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM213 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13582] As mentioned hereinabove with reference to Fig. 1, a function of VGAM213 gene, herein designated VGAM is

inhibition of expression of VGAM213 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM213 correlate with, and may be deduced from, the identity of the target genes which VGAM213 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13583] KIAA1229 (Accession XM_030665) is a VGAM213 host target gene. KIAA1229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1229 BINDING SITE, designated SEQ ID:31098, to the nucleotide sequence of VGAM213 RNA, herein designated VGAM RNA, also designated SEQ ID:2924.

[13584] A function of VGAM213 is therefore inhibition of KIAA1229 (Accession XM_030665). Accordingly, utilities of VGAM213 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1229. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 214 (VGAM214) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13585] VGAM214 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM214 was detected is described hereinabove with reference to Figs. 1–8.

[13586] VGAM214 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Autographa Californica Nucleopolyhedrovirus. VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13587] VGAM214 gene encodes a VGAM214 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM214 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM214 precursor RNA is designated SEQ ID:200, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:200 is located at position 124772 relative to the genome of Autographa Californica Nucleopolyhedrovirus.

[13588] VGAM214 precursor RNA folds onto itself, forming VGAM214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13589] An enzyme complex designated DICER COMPLEX, `dices` the VGAM214 folded precursor RNA into VGAM214 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM214 RNA is designated SEQ ID:2925, and is provided hereinbelow with reference to the sequence listing part.

[13590] VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM214 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM214 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13591] VGAM214 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM214 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM214 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[13592] The complementary binding of VGAM214 RNA, herein designated VGAM RNA, to host target binding sites on VGAM214 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM214 host target RNA into VGAM214 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13593] It is appreciated that VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM214 host target genes. The mRNA of each one of this plurality of VGAM214 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM214 RNA, herein designated VGAM RNA, and which when bound by VGAM214 RNA causes inhibition of translation of respective one or more VGAM214 host target proteins.

[13594] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM214 gene, herein designated VGAM GENE, on one or more VGAM214 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13595] It is yet further appreciated that a function of VGAM214 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM214 include diagnosis, prevention and treatment of viral infection by Autographa Californica Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM214 correlate with, and may be deduced

from, the identity of the host target genes which VGAM214 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13596] Nucleotide sequences of the VGAM214 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM214 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM214 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM214 are further described hereinbelow with reference to Table 1.

[13597] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM214 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM214 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13598] As mentioned hereinabove with reference to Fig. 1, a function of VGAM214 gene, herein designated VGAM is inhibition of expression of VGAM214 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM214 correlate with, and may be deduced from, the identity of the target genes which VGAM214

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13599] Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_133631) is a VGAM214 host target gene. ROBO1 BINDING SITE1 and ROBO1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ROBO1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROBO1 BINDING SITE1 and ROBO1 BINDING SITE2, designated SEQ ID:28583 and SEQ ID:8848 respectively, to the nucleotide sequence of VGAM214 RNA, herein designated VGAM RNA, also designated SEQ ID:2925.

[13600] A function of VGAM214 is therefore inhibition of Roundabout, Axon Guidance Receptor, Homolog 1 (Drosophila) (ROBO1, Accession NM_133631), a gene which is an axon guidance receptor. Accordingly, utilities of VGAM214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROBO1. The function of ROBO1 and its association with various diseases and clinical conditions, has been established by previous studies,

as described hereinabove with reference to VGAM37.LOC92568 (Accession XM_045852) is another VGAM214 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34576, to the nucleotide sequence of VGAM214 RNA, herein designated VGAM RNA, also designated SEQ ID:2925.

[13601] Another function of VGAM214 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM214 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 215 (VGAM215) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13602] VGAM215 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM215 was detected is described hereinabove with reference to Figs. 1–8.

[13603] VGAM215 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Autographa Californica Nucleopolyhedrovirus. VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13604] VGAM215 gene encodes a VGAM215 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM215 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM215 precursor RNA is designated SEQ ID:201, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:201 is located at position 123142 relative to the genome of Autographa Californica Nucleopolyhedrovirus.

[13605] VGAM215 precursor RNA folds onto itself, forming VGAM215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13606] An enzyme complex designated DICER COMPLEX, `dices` the VGAM215 folded precursor RNA into VGAM215 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM215 RNA is designated SEQ ID:2926, and is provided hereinbelow with reference to the sequence listing part.

[13607] VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM215 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13608] VGAM215 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM215 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM215 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13609] The complementary binding of VGAM215 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM215 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM215 host target RNA into VGAM215 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13610] It is appreciated that VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM215 host target genes. The mRNA of each one of this plurality of VGAM215 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM215 RNA, herein designated VGAM RNA, and which when bound by VGAM215 RNA causes inhibition of translation of respective one or more VGAM215 host target proteins.

[13611] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM215 gene, herein designated VGAM GENE, on one or more VGAM215 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13612] It is yet further appreciated that a function of VGAM215 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of viral infection by Autographa Californica Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM215 correlate with, and may be deduced from, the identity of the host target genes which VGAM215 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13613] Nucleotide sequences of the VGAM215 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM215 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM215 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM215 are further described hereinbelow with reference to Table 1.

[13614] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM215 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM215 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13615] As mentioned hereinabove with reference to Fig. 1, a function of VGAM215 gene, herein designated VGAM is inhibition of expression of VGAM215 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM215 correlate with, and may be deduced from, the identity of the target genes which VGAM215 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13616] HLA-B Associated Transcript 1 (BAT1, Accession NM_080598) is a VGAM215 host target gene. BAT1 BINDING SITE1 and BAT1 BINDING SITE2 are HOST TARGET

binding sites found in untranslated regions of mRNA encoded by BAT1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAT1 BINDING SITE1 and BAT1 BINDING SITE2, designated SEQ ID:27907 and SEQ ID:11014 respectively, to the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, also designated SEQ ID:2926.

[13617] A function of VGAM215 is therefore inhibition of HLA-B Associated Transcript 1 (BAT1, Accession NM_080598), a gene which associates with the major histocompatibility complex, a negative regulator of inflammation. Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAT1. The function of BAT1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM55. Ubiquitin-conjugating Enzyme E2L 3 (UBE2L3, Accession NM_003347) is another VGAM215 host target gene. UBE2L3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2L3, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2L3 BINDING SITE, designated SEQ ID:9355, to the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, also designated SEQ ID:2926.

[13618] Another function of VGAM215 is therefore inhibition of Ubiquitin-conjugating Enzyme E2L 3 (UBE2L3, Accession NM_003347), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2L3. The function of UBE2L3 has been established by previous studies. Shimura et al. (2001) hypothesized that alpha-synuclein (OMIM Ref. No. 163890) and parkin (OMIM Ref. No. 602544) interact functionally, namely, that parkin ubiquitinates alpha-synuclein normally and that this process is altered in autosomal recessive Parkinson disease (OMIM Ref. No. 600116). Shimura et al. (2001) identified a protein complex in normal human brain that includes parkin as the E3 ubiquitin ligase, UBCH7 as its associated E2 ubiquitin-conjugating enzyme, and a novel 22-kD glycosylated form of alpha-synuclein (alpha-Sp22)

as its substrate. In contrast to normal parkin, mutant parkin associated with autosomal recessive Parkinson disease failed to bind alpha-Syn22. In an in vitro ubiquitination assay, alpha-Syn22 was modified by normal, but not mutant, parkin into polyubiquitinated, high molecular weight species. Accordingly, alpha-Syn22 accumulated in a nonubiquitinated form in parkin-deficient Parkinson disease brains. Shimura et al. (2001) concluded that alpha-Syn22 is a substrate for parkin's ubiquitin ligase activity in normal human brain and that loss of parkin function causes pathologic accumulation of alpha-Syn22. These findings demonstrated a critical biochemical reaction between the 2 Parkinson disease-linked gene products and suggested that this reaction underlies the accumulation of ubiquitinated alpha-synuclein in conventional Parkinson disease. By RT-PCR, Moynihan et al. (1998) determined that UBE2L3 is expressed as 4 mRNAs that differ in the length of the 3-prime untranslated region (UTR). Sequence comparisons revealed that the human and mouse UBE2L3 cDNAs share 97% DNA sequence identity in the coding region and 93% identity for 287 nucleotides extending into the 3-prime UTR. The predicted mouse and human UBE2L3 proteins are identical.

- [13619] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [13620] Moynihan, T. P.; Cole, C. G.; Dunham, I.; O'Neil, L.; Markham, A. F.; Robinson, P. A. : Fine-mapping, genomic organization, and transcript analysis of the human ubiquitin-conjugating enzyme gene UBE2L3. *Genomics* 51: 124-127, 1998. ; and
- [13621] Shimura, H.; Schlossmacher, M. G.; Hattori, N.; Frosch, M. P.; Trockenbacher, A.; Schneider, R.; Mizuno, Y.; Kosik, K. S.; Selkoe, D. J. : Ubiquitination of a new form of alpha-synuclei.
- [13622] Further studies establishing the function and utilities of UBE2L3 are found in John Hopkins OMIM database record ID 603721, and in cited publications numbered 5363, 834 and 6191 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0391 (Accession NM_014672) is another VGAM215 host target gene. KIAA0391 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0391, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of KIAA0391 BINDING SITE, designated SEQ ID:16139, to the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, also designated SEQ ID:2926.

[13623] Another function of VGAM215 is therefore inhibition of KIAA0391 (Accession NM_014672). Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0391. RAB20, Member RAS Oncogene Family (RAB20, Accession NM_017817) is another VGAM215 host target gene. RAB20 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB20 BINDING SITE, designated SEQ ID:19463, to the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, also designated SEQ ID:2926.

[13624] Another function of VGAM215 is therefore inhibition of RAB20, Member RAS Oncogene Family (RAB20, Accession NM_017817). Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with RAB20. Solute Carrier Family 12, (potassium–chloride transporter) Member 5 (SLC12A5, Accession NM_020708) is another VGAM215 host target gene. SLC12A5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SLC12A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC12A5 BINDING SITE, designated SEQ ID:21855, to the nucleotide sequence of VGAM215 RNA, herein designated VGAM RNA, also designated SEQ ID:2926.

[13625] Another function of VGAM215 is therefore inhibition of Solute Carrier Family 12, (potassium–chloride transporter) Member 5 (SLC12A5, Accession NM_020708). Accordingly, utilities of VGAM215 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC12A5. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 216 (VGAM216) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes

is known in the art.

[13626] VGAM216 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM216 was detected is described hereinabove with reference to Figs. 1–8.

[13627] VGAM216 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Leukosis Virus. VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13628] VGAM216 gene encodes a VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM216 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM216 precursor RNA is designated SEQ ID:202, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:202 is located at position 1866 relative to the genome of Avian Leukosis Virus.

[13629] VGAM216 precursor RNA folds onto itself, forming VGAM216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[13630] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM216 folded precursor RNA into VGAM216 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 75%) nucleotide se-
quence of VGAM216 RNA is designated SEQ ID:2927, and
is provided hereinbelow with reference to the sequence
listing part.

[13631] VGAM216 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM216 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM216 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[13632] VGAM216 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM216 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM216 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[13633] The complementary binding of VGAM216 RNA, herein designated VGAM RNA, to host target binding sites on VGAM216 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM216 host target RNA into VGAM216 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13634] It is appreciated that VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM216 host target genes. The mRNA of each one of this plurality of VGAM216 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM216 RNA, herein designated VGAM RNA, and which when bound by VGAM216 RNA causes inhibition of translation of respective one or more VGAM216 host target proteins.

[13635] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM216 gene, herein designated VGAM GENE, on one or

more VGAM216 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13636] It is yet further appreciated that a function of VGAM216 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of viral infection by Avian Leukosis Virus. Specific functions, and accordingly utilities, of VGAM216 correlate with, and may be deduced from, the identity of the host target genes which VGAM216 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [13637] Nucleotide sequences of the VGAM216 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM216 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM216 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM216 are further described hereinbelow with reference to Table 1.
- [13638] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM216 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM216 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [13639] As mentioned hereinabove with reference to Fig. 1, a function of VGAM216 gene, herein designated VGAM is inhibition of expression of VGAM216 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM216 correlate with, and may be deduced from, the identity of the target genes which VGAM216 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [13640] Egl Nine Homolog 1 (C. elegans) (EGLN1, Accession

NM_022051) is a VGAM216 host target gene. EGLN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGLN1 BINDING SITE, designated SEQ ID:22584, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13641] A function of VGAM216 is therefore inhibition of Egl Nine Homolog 1 (*C. elegans*) (EGLN1, Accession NM_022051), a gene which is expressed in the cytoplasm of arterial smooth muscle cells. Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN1. The function of EGLN1 has been established by previous studies. HIF is a transcriptional complex that plays a central role in mammalian oxygen homeostasis. Posttranslational modification by prolyl hydroxylation is a key regulatory event that targets HIF- α (HIF1; 603348) subunits for proteasomal destruction via the von Hippel-Lindau (VHL; 193300) ubiquitylation complex. Epstein et al. (2001) defined a conserved HIF-VHL-prolyl hydroxylase pathway in

C. elegans and identified Egl9 as a dioxygenase that regulates HIF by prolyl hydroxylation. In mammalian cells, they showed that the HIF-prolyl hydroxylases are represented by 3 proteins with a conserved 2-histidine-1-carboxylate iron coordination motif at the catalytic site. The genes encoding these proteins were cloned and termed PHD1 (OMIM Ref. No. 606424), PHD2, and PHD3 (OMIM Ref. No. 606426) by the authors. Direct modulation of recombinant enzyme activity by graded hypoxia, iron chelation, and cobaltous ions mirrored the characteristics of HIF induction in vivo, fulfilling requirements for these enzymes being oxygen sensors that regulate HIF. In cultured mammalian cells, Bruick and McKnight (2001) found that the inappropriate accumulation of HIF caused by forced expression of the HIF1-alpha (OMIM Ref. No. 603348) subunit under normoxic conditions was attenuated by coexpression of HPH. Suppression of HPH in cultured *Drosophila melanogaster* cells by RNA interference resulted in elevated expression of the hypoxia-inducible gene LDH (see OMIM Ref. No. 150000) under normoxic conditions. Bruick and McKnight (2001) concluded that HPH is an essential component of the pathway through which cells sense oxygen.

[13642] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13643] Bruick, R. K.; McKnight, S. L. : A conserved family of prolyl-4-hydroxylases that modify HIF. Science 294: 1337-1340, 2001. ; and

[13644] Epstein, A. C. R.; Gleadle, J. M.; McNeill, L. A.; Hewitson, K. S.; O'Rourke, J.; Mole, D. R.; Mukherji, M.; Metzen, E.; Wilson, M. I.; Dhanda, A.; Tian, Y.-M.; Masson, N.; Hamilton.

[13645] Further studies establishing the function and utilities of EGLN1 are found in John Hopkins OMIM database record ID 606425, and in cited publications numbered 454 and 4545 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 2 (RPS6KA2, Accession NM_021135) is another VGAM216 host target gene.

RPS6KA2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RPS6KA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPS6KA2 BINDING SITE, designated SEQ ID:22105, to the nucleotide sequence of VGAM216 RNA,

herein designated VGAM RNA, also designated SEQ ID:2927.

[13646] Another function of VGAM216 is therefore inhibition of Ribosomal Protein S6 Kinase, 90kDa, Polypeptide 2 (RPS6KA2, Accession NM_021135), a gene which phosphorylates a wide range of substrates including ribosomal protein s6. Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPS6KA2. The function of RPS6KA2 has been established by previous studies. Serine/threonine protein kinases in the ribosomal S6 kinase (RSK) family have been implicated as signaling intermediates in the cellular response to several growth factors. Moller et al. (1994) described the cloning and characterization of 3 genes encoding 3 isoforms of ribosomal protein S6 kinase, which they called HU1 (RPS6KA1; 601684), HU2 (RPS6KA2), and HU3 (RPS6KA3; 300075). The partial HU2 cDNA (GenBank L07598) encodes a predicted protein containing 2 distinct consensus ATP-binding site sequences. Northern blot and RNase protection analyses detected major 7.5-kb and minor 3.5-kb HU2 transcripts in fibroblasts, skeletal muscle, lymphocytes, and placenta. Zhao et al. (1995) cloned a full-length cDNA encoding the

RPS6KA2 isoform of ribosomal protein S6 kinase, which they designated RSK3. The deduced 733–amino acid RSK3 protein has 84% and 75% sequence identity with RSK2 (RPS6KA3) and RSK1 (RPS6KA1), respectively. RSK3 has a unique N–terminal sequence which contains a putative bipartite nuclear localization signal. Immunoblot analysis of human cell lysates detected an 83–kD RSK protein. The authors demonstrated serum–stimulated nuclear translocation of endogenous RSK3 in HeLa cells. RSK3 exhibited growth–stimulated autophosphorylation and kinase activity; however, its relative activity toward several known RSK substrates differed from the activities of other RSKs. Unlike RSK1, RSK3 was not activated by ERK2 (PRKM1; 176948) in vitro. Northern blot analysis detected a single 6.5–kb RSK3 transcript in all tissues examined, with the highest expression in lung and skeletal muscle.

[13647] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13648] Moller, D. E.; Xia, C. H.; Tang, W.; Zhu, A. X.; Jakubowski, M. : Human rsk isoforms: cloning and characterization of tissue–specific expression. *Am. J. Physiol.* 266: C351–C359, 1994. ; and

[13649] Zhao, Y.; Bjorbaek, C.; Weremowicz, S.; Morton, C. C.; Moller, D. E. : RSK3 encodes a novel pp90rsk isoform with a unique N-terminal sequence: growth factor-stimulated kinase function and n.

[13650] Further studies establishing the function and utilities of RPS6KA2 are found in John Hopkins OMIM database record ID 601685, and in cited publications numbered 622 and 9211-9212 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glucocorticoid Modulatory Element Binding Protein 2 (GMEB2, Accession NM_012384) is another VGAM216 host target gene. GMEB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GMEB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GMEB2 BINDING SITE, designated SEQ ID:14740, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13651] Another function of VGAM216 is therefore inhibition of Glucocorticoid Modulatory Element Binding Protein 2 (GMEB2, Accession NM_012384). Accordingly, utilities of

VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GMEB2. HS6ST (Accession XM_030529) is another VGAM216 host target gene. HS6ST BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS6ST, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HS6ST BINDING SITE, designated SEQ ID:31072, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13652] Another function of VGAM216 is therefore inhibition of HS6ST (Accession XM_030529). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS6ST. Heparan Sulfate 6-O-sulfotransferase 1 (HS6ST1, Accession NM_004807) is another VGAM216 host target gene. HS6ST1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HS6ST1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of HS6ST1 BINDING SITE, designated SEQ ID:11230, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13653] Another function of VGAM216 is therefore inhibition of Heparan Sulfate 6-O-sulfotransferase 1 (HS6ST1, Accession NM_004807). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HS6ST1. KIAA0339 (Accession XM_049380) is another VGAM216 host target gene. KIAA0339 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0339, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0339 BINDING SITE, designated SEQ ID:35404, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13654] Another function of VGAM216 is therefore inhibition of KIAA0339 (Accession XM_049380). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0339. LOC115051 (Accession XM_010647) is another VGAM216 host target gene. LOC115051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC115051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115051 BINDING SITE, designated SEQ ID:30160, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13655] Another function of VGAM216 is therefore inhibition of LOC115051 (Accession XM_010647). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115051. LOC123096 (Accession XM_058679) is another VGAM216 host target gene. LOC123096 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC123096, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123096 BINDING SITE, designated SEQ ID:36721, to the nucleotide sequence of VGAM216 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2927.

[13656] Another function of VGAM216 is therefore inhibition of LOC123096 (Accession XM_058679). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123096. LOC220549 (Accession XM_167521) is another VGAM216 host target gene. LOC220549 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220549, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220549 BINDING SITE, designated SEQ ID:44652, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13657] Another function of VGAM216 is therefore inhibition of LOC220549 (Accession XM_167521). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220549. LOC253100 (Accession XM_174623) is another VGAM216 host target gene. LOC253100 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253100, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253100 BINDING SITE, designated SEQ ID:46600, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13658] Another function of VGAM216 is therefore inhibition of LOC253100 (Accession XM_174623). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253100. LOC51054 (Accession NM_015899) is another VGAM216 host target gene. LOC51054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51054 BINDING SITE, designated SEQ ID:18042, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13659] Another function of VGAM216 is therefore inhibition of LOC51054 (Accession NM_015899). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC51054. LOC84661 (Accession NM_032574) is another VGAM216 host target gene. LOC84661 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC84661, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC84661 BINDING SITE, designated SEQ ID:26303, to the nucleotide sequence of VGAM216 RNA, herein designated VGAM RNA, also designated SEQ ID:2927.

[13660] Another function of VGAM216 is therefore inhibition of LOC84661 (Accession NM_032574). Accordingly, utilities of VGAM216 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC84661. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 217 (VGAM217) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13661] VGAM217 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM217 was detected is described hereinabove with reference to Figs. 1–8.

[13662] VGAM217 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Avian Leukosis Virus. VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13663] VGAM217 gene encodes a VGAM217 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM217 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM217 precursor RNA is designated SEQ ID:203, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:203 is located at position 3402 relative to the genome of Avian Leukosis Virus.

[13664] VGAM217 precursor RNA folds onto itself, forming VGAM217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13665] An enzyme complex designated DICER COMPLEX, `dices` the VGAM217 folded precursor RNA into VGAM217 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM217 RNA is designated SEQ ID:2928, and is provided hereinbelow with reference to the sequence listing part.

[13666] VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM217 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13667] VGAM217 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM217 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM217 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13668] The complementary binding of VGAM217 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM217 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM217 host target RNA into VGAM217 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13669] It is appreciated that VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM217 host target genes. The mRNA of each one of this plurality of VGAM217 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM217 RNA, herein designated VGAM RNA, and which when bound by VGAM217 RNA causes inhibition of translation of respective one or more VGAM217 host target proteins.

[13670] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM217 gene, herein designated VGAM GENE, on one or more VGAM217 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13671] It is yet further appreciated that a function of VGAM217 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of viral infection by Avian Leukosis Virus. Specific functions, and accordingly utilities, of VGAM217 correlate with, and may be deduced from, the identity of the host target genes which VGAM217 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13672] Nucleotide sequences of the VGAM217 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

5' duced 5' VGAM217 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM217 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM217 are further described hereinbelow with reference to Table 1.

[13673] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM217 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM217 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13674] As mentioned hereinabove with reference to Fig. 1, a function of VGAM217 gene, herein designated VGAM is inhibition of expression of VGAM217 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM217 correlate with, and may be deduced from, the identity of the target genes which VGAM217 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13675] Activin A Receptor, Type I (ACVR1, Accession NM_001105) is a VGAM217 host target gene. ACVR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by ACVR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACVR1 BINDING SITE, designated SEQ ID:6761, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13676] A function of VGAM217 is therefore inhibition of Activin A Receptor, Type I (ACVR1, Accession NM_001105), a gene which Activin receptor-like kinase; similar to activin, TGF-beta, and C. elegans daf-1 receptors. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACVR1. The function of ACVR1 has been established by previous studies. See ACVRLK1 (OMIM Ref. No. 601284). Although activins were discovered by virtue of their capacity to stimulate the production of follicle-stimulating hormone (FSH; 136530) by the pituitary gland and inhibins were initially characterized as FSH inhibitors, activins and inhibins are dimeric proteins that share a common subunit. There are 3 activins (A, B, and A-B), comprising different combinations of 2 closely related beta subunits (beta-A/beta-A; beta-B/beta-B; and beta-A/beta-B, re-

spectively) and 2 inhibins (A and B), consisting of 1 beta-subunit and an inhibin-specific alpha subunit (alpha/beta-A and alpha/beta-B). Activins impinge on a much broader spectrum of cells than do inhibins; however, in those systems in which both proteins are functional, they have opposing biologic effects. Activins are members of a family of polypeptide growth factors that includes also the transforming growth factors-beta (190180, 190220, 190230), mullerian duct-inhibiting substance, and several bone morphogenetic proteins. Human cDNA clones encoding 4 putative transmembrane ser/thr kinases were identified by ten Dijke et al. (1993). By Southern blot analysis of DNAs from a somatic cell hybrid mapping panel, Roijer et al. (1998) mapped the ACVR1 gene to chromosome 2. By fluorescence in situ hybridization, they regionalized the gene to 2q23-q24.

[13677] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13678] ten Dijke, P.; Ichijo, H.; Franzen, P.; Schulz, P.; Saras, J.; Toyoshima, H.; Heldin, C.-H.; Miyazono, K. : Activin receptor-like kinases: a novel subclass of cell-surface receptors with predicted serine/threonine kinase activity.

Oncogene 8: 2879–2887, 1993. ; and

[13679] Roijer, E.; Miyazono, K.; Astrom, A.–K.; Geurts van Kessel, A.; ten Dijke, P.; Stenman, G. : Chromosomal localization of three human genes encoding members of the TGF–beta superfamily of.

[13680] Further studies establishing the function and utilities of ACVR1 are found in John Hopkins OMIM database record ID 102576, and in cited publications numbered 4267–4271 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dihydropyrimidinase–like 2 (DPYSL2, Accession NM_001386) is another VGAM217 host target gene. DPYSL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DPYSL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DPYSL2 BINDING SITE, designated SEQ ID:7062, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13681] Another function of VGAM217 is therefore inhibition of Dihydropyrimidinase–like 2 (DPYSL2, Accession

NM_001386), a gene which is a member of the dihydropyrimidinase family. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYSL2. The function of DPYSL2 has been established by previous studies.

Hamajima et al. (1996) isolated a human cDNA encoding dihydropyrimidinase-like 2 (OMIM Ref. No. DPYSL2), called DRP2 by them, from a fetal brain cDNA library (see OMIM Ref. No. 222748). The DPYSL2 protein has 572 amino acids. Northern blot analysis detected a 4.9-kb DPYSL2 transcript in all tissues examined except liver. Hamajima et al. (1996) noted that 3 ESTs mapped to 8p21 by Koyama et al. (1995) correspond to a portion of the coding region of DPYSL2.

[13682] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13683] Hamajima, N.; Matsuda, K.; Sakata, S.; Tamaki, N.; Sasaki, M.; Nonaka, M. : A novel gene family defined by human dihydropyrimidinase and three related proteins with differential tissue distribution. Gene 180: 157-163, 1996. ; and

[13684] Koyama, K.; Sudo, K.; Nakamura, Y. : Isolation of 115 hu-

man chromosome 8-specific expressed-sequence tags by exon amplification. Genomics 26: 245-253, 1995.

[13685] Further studies establishing the function and utilities of DPYSL2 are found in John Hopkins OMIM database record ID 602463, and in cited publications numbered 327 and 6187 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Forkhead Box F2 (FOXF2, Accession NM_001452) is another VGAM217 host target gene. FOXF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXF2 BINDING SITE, designated SEQ ID:7186, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13686] Another function of VGAM217 is therefore inhibition of Forkhead Box F2 (FOXF2, Accession NM_001452), a gene which is a probable transcription activator for a number of lung-specific genes. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXF2. The func-

tion of FOXF2 has been established by previous studies. The forkhead domain is a 100–amino acid monomeric DNA binding motif originally identified as a region of homology between the *Drosophila* forkhead protein and rat HNF3. Pierrou et al. (1994) identified 7 human genes containing forkhead domains and designated them forkhead related activators (FREAC) 1 through 7. Northern blot analysis revealed that the FREAC2, or FKHL6, gene is expressed as a 2.4–kb mRNA primarily in placenta and adult and fetal lung. Pierrou et al. (1994) determined the DNA binding specificity of FKHL6 through selection of high-affinity binding sites from random sequence oligonucleotides. Hellqvist et al. (1996) reported the sequence of a partial FREAC2 cDNA. The predicted 408–amino acid protein is missing the N-terminal region. Sequence analysis revealed that the FREAC1 (FKHL5; 601089) and FREAC2 proteins are nearly identical within a 112–residue region containing the forkhead domain and adjacent sequences, and within the C-terminal region. Using a reporter gene construct containing in the promoter the FREAC2 binding sequences identified by Pierrou et al. (1994), Hellqvist et al. (1996) demonstrated that both FREAC1 and FREAC2 have C-terminal transcriptional activation domains.

FREAC1/FREAC2 binding sequences are present in the promoters of several lung-specific genes, including CC10 (OMIM Ref. No. 192020) and SPB (SFTPBB; 178640). Both FREAC1 and FREAC2 transactivated an SPB promoter construct. Blixt et al. (1998) reported that the full-length FREAC2 protein contains 444 amino acids.

[13687] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13688] Hellqvist, M.; Mahlapuu, M.; Samuelsson, L.; Enerback, S.; Carlsson, P. : Differential activation of lung-specific genes by two forkhead proteins, FREAC-1 and FREAC-2. J. Biol. Chem. 271: 4482-4490, 1996. ; and

[13689] Pierrou, S.; Hellqvist, M.; Samuelsson, L.; Enerback, S.; Carlsson, P. : Cloning and characterization of seven human forkhead proteins: binding site specificity and DNA bending. EMBO J.

[13690] Further studies establishing the function and utilities of FOXF2 are found in John Hopkins OMIM database record ID 603250, and in cited publications numbered 8656, 9457-945 and 9460 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. MAD, Mothers Against Decapentaplegic Homolog 4

(Drosophila) (MADH4, Accession NM_005359) is another VGAM217 host target gene. MADH4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MADH4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MADH4 BINDING SITE, designated SEQ ID:11829, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13691] Another function of VGAM217 is therefore inhibition of MAD, Mothers Against Decapentaplegic Homolog 4 (Drosophila) (MADH4, Accession NM_005359), a gene which common mediator of signal transduction by $\text{tgf-}\beta$ (transforming growth factor) superfamily; smad4 is the common smad (co-smad). promotes binding of the smad2/smad4/fast-1 complex to dna and provides an activation function required for smad1 or smad2 to stimulate transcription. may act as a tumor suppressor. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MADH4. The function of MADH4 has been established by previous studies. About 90% of human pan-

creatic carcinomas show allelic loss at 18q. Hahn et al. (1996) reported the identification of a putative tumor suppressor gene on chromosome 18q21.1 that may be a candidate for pancreatic carcinoma. The gene was homozygously deleted in 25 of 84 tumors and mutations were identified as somatic mutations in 6 of 27 carcinomas that lacked deletions. The gene was localized by deletion analysis of xenograft DNA. Markers absent in these samples were used to screen the CEPH mega-YAC library. YACs spanning the minimal deletion region were subcloned as cosmids for sequencing and recovery of cDNAs. A 2,680-bp cDNA was found and shown to code for a predicted 552-amino acid protein. The predicted protein shares blocks of as much as 85% similarity to the *Drosophila* Mad protein and the *Caenorhabditis elegans* sma-2, -3 and -4 proteins. In *Drosophila*, homozygous Mad mutants exhibit a variety of developmental defects. The authors showed that the human gene contains 11 exons. Hahn et al. (1996) designated the gene DPC4 (for homozygously deleted in pancreatic carcinoma, locus 4). This region of chromosome 18q also contains a gene (DCC; 120470) found to be deleted in colorectal cancers. Animal model experiments lend further support to the

function of MADH4. Takaku et al. (1998) inactivated the mouse Dpc4 (Smad4) homolog. The homozygous mutants were embryonic lethal, whereas the heterozygotes showed no abnormality. The investigators then introduced the Dpc4 mutation into the knockout mice for the mouse homolog of the human APC (OMIM Ref. No. 175100) gene, Apc-delta716, a model for human familial adenomatous polyposis. Because both Apc and Dpc4 are located on mouse chromosome 18, they constructed compound heterozygotes carrying both mutations on the same chromosome by meiotic recombination. In such mice, intestinal polyps developed into more malignant tumors than those in the simple Apc-delta716 heterozygotes, showing an extensive stromal cell proliferation, submucosal invasion, cell type heterogeneity, and in vivo transplantability.

Takaku et al. (1998) suggested that mutations in DPC4 play a significant role in the malignant progression of colorectal tumors. Sirard et al. (1998) demonstrated that homozygous Smad4 mutant mice died before embryonic day 7.5. Mutant embryos have reduced size, fail to gastrulate or express a mesodermal marker, and show abnormal visceral endoderm development. Growth retardation of the Smad4-deficient embryos results from reduced cell prolifer-

eration rather than increased apoptosis. Aggregation of mutant Smad4 embryonic stem cells with wildtype tetraploid morulae rescued the gastrulation defect. The results of Sirard et al. (1998) indicated that Smad4 is initially required for the differentiation of the visceral endoderm and that the gastrulation defect in the epiblast is secondary and noncell autonomous. Rescued embryos showed severe anterior truncations, indicating a second important role for Smad4 in anterior patterning during embryogenesis

[13692] It is appreciated that the abovementioned animal model for MADH4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13693] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13694] Sirard, C.; de la Pompa, J. L.; Elia, A.; Itie, A.; Mirtsos, C.; Cheung, A.; Hahn, S.; Wakeham, A.; Schwartz, L.; Kern, S. E.; Rossant, J.; Mak, T. W. : The tumor suppressor gene Smad4/Dpc4 is required for gastrulation and later for anterior development of the mouse embryo. *Genes Dev.* 12: 107–119, 1998. ; and

[13695] Hahn, S. A.; Schutte, M.; Hoque, T. M. S.; Moskaluk, C. A.; da Costa, L. T.; Rozenblum, E.; Weinstein, C. L.; Fischer, A.; Yeo, C. J.; Hruban, R. H.; Kern, S. E. : DPC4, a candidate tumor s.

[13696] Further studies establishing the function and utilities of MADH4 are found in John Hopkins OMIM database record ID 600993, and in cited publications numbered 7161, 7798, 12349-7817, 10962, 10965-1096 and 7819-7832 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase 1 (MAPK1, Accession NM_002745) is another VGAM217 host target gene. MAPK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPK1 BINDING SITE, designated SEQ ID:8615, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13697] Another function of VGAM217 is therefore inhibition of Mitogen-activated Protein Kinase 1 (MAPK1, Accession NM_002745), a gene which phosphorylates microtubule-

associated protein-2 (map2). myelin basic protein (mbp), and elk-1; may promote entry in the cell cycle. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPK1. The function of MAPK1 has been established by previous studies. Forcet et al. (2002) showed that in embryonic kidney cells expressing full-length, but not cytoplasmic domain-truncated, DCC (OMIM Ref. No. 120470), NTN1 (OMIM Ref. No. 601614) causes increased transient phosphorylation and activity of ERK1 and ERK2, but not of JNK1 (OMIM Ref. No. 601158), JNK2 (OMIM Ref. No. 602896), or p38 (MAPK14; 600289). This phosphorylation was mediated by MEK1 and/or MEK2. NTN1 also activated the transcription factor ELK1 (OMIM Ref. No. 311040) and serum response element-regulated gene expression. Immunoprecipitation analysis showed interaction of full-length DCC with MEK1/2 in the presence or absence of NTN1. Forcet et al. (2002) showed that activation of Dcc by Ntn1 in rat embryonic day-13 dorsal spinal cord stimulates and is required for the outgrowth of commissural axons and Erk1/2 activation. Immunohistochemical analysis demonstrated expression of activated Erk1/2 in embryonic commissural axons, and this expression was

diminished in Dcc or Ntn1 knockout animals. Forcet et al. (2002) concluded that the MAPK pathway is involved in responses to NTN1 and proposed that ERK activation affects axonal growth by phosphorylation of microtubule-associated proteins and neurofilaments. Stefanovsky et al. (2001) showed that epidermal growth factor (OMIM Ref. No. 131530) induces immediate, ERK1/ERK2-dependent activation of endogenous ribosomal transcription, while inactivation of ERK1/ERK2 causes an equally immediate reversion to the basal transcription level. ERK1/ERK2 was found to phosphorylate the architectural transcription factor UBF (OMIM Ref. No. 600673) at amino acids 117 and 201 within HMG boxes 1 and 2, preventing their interaction with DNA. Mutation of these sites inhibited transcription activation and abrogated the transcriptional response to ERK1/ERK2. Thus, growth factor regulation of ribosomal transcription likely acts by a cyclic modulation of DNA architecture. The data suggested a central role for ribosome biogenesis in growth regulation

[13698] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13699] Forcet, C.; Stein, E.; Pays, L.; Corset, V.; Llambi, F.;

Tessier-Lavigne, M.; Mehlen, P. : Netrin-1-mediated axon outgrowth requires deleted in colorectal cancer-dependent MAPK activation. Nature 417: 443-447, 2002. ; and

[13700] Stefanovsky, V. Y.; Pelletier, G.; Hannan, R.; Gagnon-Kugler, T.; Rothblum, L. I.; Moss, T. : An immediate response of ribosomal transcription to growth factor stimulation in mammals is.

[13701] Further studies establishing the function and utilities of MAPK1 are found in John Hopkins OMIM database record ID 176948, and in cited publications numbered 1529-1532, 10346-1536, 10350, 10354-153 and 3462 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 5',3'-nucleotidase, Mitochondrial (NT5M, Accession NM_020201) is another VGAM217 host target gene. NT5M BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NT5M, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NT5M BINDING SITE, designated SEQ ID:21436, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2928.

[13702] Another function of VGAM217 is therefore inhibition of 5',3'-nucleotidase, Mitochondrial (NT5M, Accession NM_020201). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NT5M. Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM_003479) is another VGAM217 host target gene. PTP4A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTP4A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTP4A2 BINDING SITE, designated SEQ ID:9550, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13703] Another function of VGAM217 is therefore inhibition of Protein Tyrosine Phosphatase Type IVA, Member 2 (PTP4A2, Accession NM_003479), a gene which is a protein tyrosine phosphatase which has a C-terminal prenylation site. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with PTP4A2. The function of PTP4A2 has been established by previous studies. The rat Prl1 (phosphatase of regenerating liver-1; 601585) protein is a 20-kD nuclear protein tyrosine phosphatase (OMIM Ref. No. PTPase) that is not homologous to previously characterized dual-specificity PTPases or the monospecific PTPases. Montagna et al. (1995) identified a cDNA encoding a human PRL1-like protein, which they designated OV1. By using an in vitro prenylation screen, Cates et al. (1996) found that human PRL1 and OV1, which they referred to as PTP(CAAX1) and PTP(CAAX2), respectively, are farnesylated in vitro by mammalian farnesyl:protein transferase. Overexpression of these PTPs in epithelial cells caused a transformed phenotype in cultured cells and tumor growth in nude mice. Cates et al. (1996) concluded that PTP(CAAX1) and PTP(CAAX2) represent a novel class of isoprenylated, oncogenic PTPs. Zhao et al. (1996) isolated both cDNA and genomic clones as part of a screen for genes with CTG repeats. Among these were 2 cDNAs, HH13 and HH7-2, that were identical in their coding regions but differed primarily in their 5-prime untranslated regions (UTRs). The predicted 167-amino acid sequence from each was 89% identical to

rat Prl1 but was unrelated to other PTPs except for the active site. The protein contains a large number of basic residues and has a predicted isoelectric point of 8.33. Northern blot analysis using a probe from the common 3-prime UTR of HH13 and HH7-2 identified transcripts of 2 and 4 kb in all human tissues examined. Zeng et al. (1998) identified cDNAs encoding the mouse homolog of human PTP(CAAX2), or PRL2. The predicted human and mouse PRL2 proteins are identical. Zhao et al. (1996) used the HH13 cDNA to identify a YAC that was mapped to 1p35 by fluorescence in situ hybridization. They found a third cDNA (designated HH18) which contains a large deletion in the reading frame and may be a splice variant of either HH13 or HH7-2. Furthermore, a processed pseudogene with 96% sequence identity was found in the BRCA1 (OMIM Ref. No. 113705) region of 17q21.

[13704] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13705] Cates, C. A.; Michael, R. L.; Stayrook, K. R.; Harvey, K. A.; Burke, Y. D.; Randall, S. K.; Crowell, P. L.; Crowell, D. N. : Prenylation of oncogenic human PTP(CAAX) protein tyrosine phosphatases. Cancer Lett. 110: 49-55, 1996. ; and

[13706] Zhao, Z.; Lee, C.-C.; Monckton, D. G.; Yazdani, A.; Coolbaugh, M. I.; Li, X.; Bailey, J.; Shen, Y.; Caskey, C. T. : Characterization and genomic mapping of genes and pseudogenes of a new.

[13707] Further studies establishing the function and utilities of PTP4A2 are found in John Hopkins OMIM database record ID 601584, and in cited publications numbered 6551–655 and 7174 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor Type, D (PTPRD, Accession NM_130391) is another VGAM217 host target gene. PTPRD BINDING SITE1 through PTPRD BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRD BINDING SITE1 through PTPRD BINDING SITE4, designated SEQ ID:28178, SEQ ID:28179, SEQ ID:28180 and SEQ ID:8722 respectively, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13708] Another function of VGAM217 is therefore inhibition of

Protein Tyrosine Phosphatase, Receptor Type, D (PTPRD, Accession NM_130391), a gene which plays important roles in regulating hippocampal LTP and learning processes. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRD. The function of PTPRD has been established by previous studies. Mizuno et al. (1993) isolated a mouse gene that was highly homologous to human protein-tyrosine phosphatase-delta. The cDNA clones were isolated by screening mouse brain cDNA libraries with mouse CD45 protein-tyrosine phosphatase domain probes under reduced stringency. Northern blot analysis demonstrated expression of 3 mRNA species in brain, kidney, and heart. In situ hybridization of brain samples revealed that the mRNA was present in hippocampus, thalamic reticular nucleus, and piriform cortex. Although this murine mRNA was not detected in lymphoid tissues, all of the pre-B cell lines tested and 1 of 3 B-cell lines tested expressed mRNA, whereas antibody-producing B-cell hybridomas and T-cell and macrophage lines did not. Testing a panel of recombinant inbred strains, Mizuno et al. (1993) mapped the gene to mouse chromosome 4 in tight linkage to the 'brown' (b) locus.

They found that the mouse gene was closely homologous to the human PTPRD gene. A high degree of structural similarity had been demonstrated between LAR (PTPRF; 179590) in the human and human PTPRD. This raised the possibility that they are allelic forms or that PTPRD and LAR are related but distinct gene products. The findings of Mizuno et al. (1993) in the mouse supported the latter possibility. First, the LAR gene is expressed predominantly in cells of epithelial origin and T cells but not in B cells, whereas expression of murine PTP-delta is restricted to brain, kidney, heart, and some B-cell lines. Second, the chromosomal localization of LAR to human 1p34-p32 is different from the location on mouse chromosome 4, close to the b locus, which corresponds to human 9q. It is noteworthy that the Ptp rf gene maps to mouse chromosome 4 (Schaapveld et al., 1995). Animal model experiments lend further support to the function of PTPRD. Ptp rd is a receptor-type protein-tyrosine phosphatase expressed in the specialized regions of the brain, including the hippocampal CA2 and CA3, in B lymphocytes, and in the thymic medulla. To elucidate the physiologic roles of Ptp rd, Uetani et al. (2000) produced Ptp rd-deficient mice by gene targeting. They found that Ptp rd-deficient mice

were semilethal due to insufficient food intake. The mice also exhibited learning impairment in the Morris water maze, reinforced T-maze, and radial arm maze tasks. Although the histology of the hippocampus appeared normal, the magnitudes of long-term potentiation (LTP) induced at hippocampal CA1 and CA3 synapses were significantly enhanced in *Ptprd*-deficient mice, with augmented paired-pulse facilitation in the CA1 region. Uetani et al. (2000) concluded that *Ptprd* plays important roles in regulating hippocampal LTP and learning processes, and that hippocampal LTP does not necessarily positively correlate with spatial learning ability. They stated that *Ptprd* is an important regulator of synaptic plasticity and discussed the role of *Ptprd* in learning and memory

[13709] It is appreciated that the abovementioned animal model for PTPRD is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13710] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13711] Schaapveld, R. Q. J.; van den Maagdenberg, A. M. J. M.; Schepens, J. T. G.; Olde Weghuis, D.; Geurts van Kessel,

A.; Wieringa, B.; Hendriks, W. J. A. J. : The mouse gene Pt-prf encoding the leukocyte common antigen-related molecule LAR: cloning, characterization, and chromosomal localization. Genomics 27: 124-130, 1995. ; and

[13712] Uetani, N.; Kato, K.; Ogura, H.; Mizuno, K.; Kawano, K.; Mikoshiba, K.; Yakura, H.; Asano, M.; Iwakura, Y. : Impaired learning with enhanced hippocampal long-term potentiation in PTP-del.

[13713] Further studies establishing the function and utilities of PTPRD are found in John Hopkins OMIM database record ID 601598, and in cited publications numbered 933 and 12389 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Replication Factor C (activator 1) 1, 145kDa (RFC1, Accession NM_002913) is another VGAM217 host target gene. RFC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFC1 BINDING SITE, designated SEQ ID:8820, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13714] Another function of VGAM217 is therefore inhibition of Replication Factor C (activator 1) 1, 145kDa (RFC1, Accession NM_002913), a gene which plays a role in dna transcription, replication and/or repair. Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFC1. The function of RFC1 has been established by previous studies. Replication factor C is a multisubunit, DNA polymerase accessory protein required for the coordinated synthesis of both DNA strands during simian virus 40 DNA replication in vitro. It is a DNA-dependent ATPase that binds in a structure-specific manner to the 3-prime end of a primer hybridized to a template DNA, an activity thought intrinsic to the 140-kD component of this multisubunit complex. Bunz et al. (1993) isolated and analyzed cDNAs encoding the 140-kD subunit. An open reading frame of 3.4 kb was predicted to encode a 1,148-amino acid protein with a predicted molecular mass of 130 kD. A putative ATP-binding motif was observed that is similar to a motif in several of the smaller subunits of RFC and in functionally homologous replication factors of bacterial and viral origin. The predicted protein showed similarities to other DNA-binding proteins. Wang et al. (2000) used

immunoprecipitation and mass spectrometry analyses to identify BRCA1 (OMIM Ref. No. 113705)-associated proteins. They found that BRCA1 is part of a large multisubunit protein complex of tumor suppressors, DNA damage sensors, and signal transducers. They named this complex BASC, for 'BRCA1-associated genome surveillance complex.' Among the DNA repair proteins identified in the complex were ATM (OMIM Ref. No. 208900), BLM (OMIM Ref. No. 604610), MSH2 (OMIM Ref. No. 120435), MSH6 (OMIM Ref. No. 600678), MLH1 (OMIM Ref. No. 120436), the RAD50 (OMIM Ref. No. 604040)-MRE11 (OMIM Ref. No. 600814)-NBS1 (OMIM Ref. No. 602667) complex, and the RFC1-RFC2 (OMIM Ref. No. 600404)-RFC4 (OMIM Ref. No. 102577) complex. Wang et al. (2000) suggested that BASC may serve as a sensor of abnormal DNA structures and/or as a regulator of the postreplication repair process.

[13715] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13716] Bunz, F.; Kobayashi, R.; Stillman, B. : cDNAs encoding the large subunit of human replication factor C. Proc. Nat. Acad. Sci. 90: 11014-11018, 1993. ; and

[13717] Wang, Y.; Cortez, D.; Yazdi, P.; Neff, N.; Elledge, S. J.; Qin, J. : BASC, a super complex of BRCA1-associated proteins involved in the recognition and repair of aberrant DNA structures.

[13718] Further studies establishing the function and utilities of RFC1 are found in John Hopkins OMIM database record ID 102579, and in cited publications numbered 12335-1233 and 7118 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434P211 (Accession NM_014549) is another VGAM217 host target gene. DKFZP434P211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P211 BINDING SITE, designated SEQ ID:15864, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13719] Another function of VGAM217 is therefore inhibition of DKFZP434P211 (Accession NM_014549). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP434P211. KIAA0354 (Accession NM_014872) is another VGAM217 host target gene. KIAA0354 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0354 BINDING SITE, designated SEQ ID:16998, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13720] Another function of VGAM217 is therefore inhibition of KIAA0354 (Accession NM_014872). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0354. KIAA0748 (Accession NM_014796) is another VGAM217 host target gene. KIAA0748 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0748, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0748 BINDING SITE, designated SEQ ID:16701, to the nucleotide sequence of VGAM217 RNA, herein designated

VGAM RNA, also designated SEQ ID:2928.

[13721] Another function of VGAM217 is therefore inhibition of KIAA0748 (Accession NM_014796). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0748. KIAA1056 (Accession NM_014894) is another VGAM217 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17043, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13722] Another function of VGAM217 is therefore inhibition of KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. KIAA1505 (Accession XM_168469) is another VGAM217 host target gene. KIAA1505 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1505, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1505 BINDING SITE, designated SEQ ID:45192, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13723] Another function of VGAM217 is therefore inhibition of KIAA1505 (Accession XM_168469). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1505. Phosphatidylserine Synthase 2 (PTDSS2, Accession NM_030783) is another VGAM217 host target gene. PTDSS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTDSS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTDSS2 BINDING SITE, designated SEQ ID:25074, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13724] Another function of VGAM217 is therefore inhibition of Phosphatidylserine Synthase 2 (PTDSS2, Accession

NM_030783). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTDSS2. RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM_032144) is another VGAM217 host target gene. RAB6C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB6C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB6C BINDING SITE, designated SEQ ID:25833, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13725] Another function of VGAM217 is therefore inhibition of RAB6C, Member RAS Oncogene Family (RAB6C, Accession NM_032144). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB6C. Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737) is another VGAM217 host target gene. RASSF2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASSF2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RASSF2 BINDING SITE, designated SEQ ID:16392, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13726] Another function of VGAM217 is therefore inhibition of Ras Association (RalGDS/AF-6) Domain Family 2 (RASSF2, Accession NM_014737). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASSF2. Syntaphilin (SNPH, Accession NM_014723) is another VGAM217 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16290, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13727] Another function of VGAM217 is therefore inhibition of Syntaphilin (SNPH, Accession NM_014723). Accordingly,

utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. Tankyrase, TRF1–interacting Ankyrin–related ADP–ribose Polymerase 2 (TNKS2, Accession NM_025235) is another VGAM217 host target gene. TNKS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TNKS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNKS2 BINDING SITE, designated SEQ ID:24911, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13728] Another function of VGAM217 is therefore inhibition of Tankyrase, TRF1–interacting Ankyrin–related ADP–ribose Polymerase 2 (TNKS2, Accession NM_025235). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNKS2. WIT–1 (Accession NM_015855) is another VGAM217 host target gene. WIT–1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by WIT–1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND–

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WIT-1 BINDING SITE, designated SEQ ID:17987, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13729] Another function of VGAM217 is therefore inhibition of WIT-1 (Accession NM_015855). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WIT-1. YKT6 (Accession NM_006555) is another VGAM217 host target gene. YKT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YKT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YKT6 BINDING SITE, designated SEQ ID:13317, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13730] Another function of VGAM217 is therefore inhibition of YKT6 (Accession NM_006555). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YKT6.

LOC150174 (Accession XM_086802) is another VGAM217 host target gene. LOC150174 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150174, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150174 BINDING SITE, designated SEQ ID:38871, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13731] Another function of VGAM217 is therefore inhibition of LOC150174 (Accession XM_086802). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150174. LOC150213 (Accession XM_059324) is another VGAM217 host target gene. LOC150213 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150213, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150213 BINDING SITE, designated SEQ ID:36955, to the nucleotide sequence of VGAM217 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2928.

[13732] Another function of VGAM217 is therefore inhibition of LOC150213 (Accession XM_059324). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150213. LOC150236 (Accession XM_086824) is another VGAM217 host target gene. LOC150236 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150236, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150236 BINDING SITE, designated SEQ ID:38904, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13733] Another function of VGAM217 is therefore inhibition of LOC150236 (Accession XM_086824). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150236. LOC158450 (Accession XM_088580) is another VGAM217 host target gene. LOC158450 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158450, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158450 BINDING SITE, designated SEQ ID:39841, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13734] Another function of VGAM217 is therefore inhibition of LOC158450 (Accession XM_088580). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158450. LOC158504 (Accession XM_088591) is another VGAM217 host target gene. LOC158504 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158504 BINDING SITE, designated SEQ ID:39852, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13735] Another function of VGAM217 is therefore inhibition of LOC158504 (Accession XM_088591). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC158504. LOC158677 (Accession XM_098976) is another VGAM217 host target gene. LOC158677 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC158677, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158677 BINDING SITE, designated SEQ ID:42022, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13736] Another function of VGAM217 is therefore inhibition of LOC158677 (Accession XM_098976). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158677. LOC219347 (Accession XM_167564) is another VGAM217 host target gene. LOC219347 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC219347, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219347 BINDING SITE, designated SEQ ID:44676, to

the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13737] Another function of VGAM217 is therefore inhibition of LOC219347 (Accession XM_167564). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219347. LOC222962 (Accession XM_167291) is another VGAM217 host target gene. LOC222962 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222962, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222962 BINDING SITE, designated SEQ ID:44626, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13738] Another function of VGAM217 is therefore inhibition of LOC222962 (Accession XM_167291). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222962. LOC245811 (Accession XM_168197) is another VGAM217 host target gene. LOC245811 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC245811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC245811 BINDING SITE, designated SEQ ID:45071, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13739] Another function of VGAM217 is therefore inhibition of LOC245811 (Accession XM_168197). Accordingly, utilities of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC245811. LOC254826 (Accession XM_173188) is another VGAM217 host target gene. LOC254826 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254826 BINDING SITE, designated SEQ ID:46433, to the nucleotide sequence of VGAM217 RNA, herein designated VGAM RNA, also designated SEQ ID:2928.

[13740] Another function of VGAM217 is therefore inhibition of LOC254826 (Accession XM_173188). Accordingly, utilities

of VGAM217 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254826. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 218 (VGAM218) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13741] VGAM218 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM218 was detected is described hereinabove with reference to Figs. 1–8.

[13742] VGAM218 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Leukemia Virus. VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13743] VGAM218 gene encodes a VGAM218 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM218 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM218 precursor RNA is designated SEQ ID:204, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:204 is located at position 6277 relative to the genome of Bovine Leukemia Virus.

[13744] VGAM218 precursor RNA folds onto itself, forming VGAM218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13745] An enzyme complex designated DICER COMPLEX, `dices` the VGAM218 folded precursor RNA into VGAM218 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 48%) nucleotide sequence of VGAM218 RNA is designated SEQ ID:2929, and

is provided hereinbelow with reference to the sequence listing part.

[13746] VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM218 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13747] VGAM218 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM218 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM218 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13748] The complementary binding of VGAM218 RNA, herein designated VGAM RNA, to host target binding sites on VGAM218 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM218 host target RNA into VGAM218 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13749] It is appreciated that VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM218 host target genes. The mRNA of each one of this plurality of VGAM218 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM218 RNA, herein designated VGAM RNA, and which when bound by VGAM218 RNA causes inhibition of translation of respective one or more VGAM218 host target proteins.

[13750] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM218 gene, herein designated VGAM GENE, on one or more VGAM218 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13751] It is yet further appreciated that a function of VGAM218 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM218 include diagnosis, prevention and treatment of viral infection by Bovine Leukemia Virus. Specific functions, and accordingly utilities, of VGAM218 correlate with, and may be deduced from, the identity of the host target genes which VGAM218 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13752] Nucleotide sequences of the VGAM218 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM218 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM218 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM218 are further described hereinbelow with reference to Table 1.

[13753] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM218 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM218 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13754] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM218 gene, herein designated VGAM is inhibition of expression of VGAM218 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM218 correlate with, and may be deduced from, the identity of the target genes which VGAM218 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13755] Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_000109) is a VGAM218 host target gene. DMD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DMD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE, designated SEQ ID:5571, to the nucleotide sequence of VGAM218 RNA, herein designated VGAM RNA, also designated SEQ ID:2929.

[13756] A function of VGAM218 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_000109), a gene which muscular dystrophy . Accordingly, utilities of VGAM218 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD has

been established by previous studies. Roberts et al. (1992) described a general approach to the identification of the basic defect in the one-third of DMD patients who do not show a gross rearrangement of the dystrophin gene. The method involved nested amplification, chemical mismatched detection, and sequencing of reverse transcripts of trace amounts of dystrophin mRNA from peripheral blood lymphocytes. Analysis of the entire coding region (11 kb) in 7 patients resulted in detection of a sequence change in each case that was clearly sufficient to cause the disease. All the mutations were expected to cause premature translation termination, and the resulting phenotypes were thus equivalent to those caused by frameshifting deletions; see 300377.0003–300377.0009. Deletions and point mutations in the DMD gene cause either DMD or the milder Becker muscular dystrophy, depending on whether the translational reading frame is lost or maintained. De Angelis et al. (2002) reasoned that because internal in-frame deletions in the protein produce only mild myopathic symptoms, a partially corrected phenotype could be restored by preventing the inclusion of specific mutated exons in the mature dystrophin mRNA. Such control had previously been accomplished by the use

of synthetic oligonucleotides. To circumvent the disadvantageous necessity for periodic administration of the synthetic oligonucleotides, De Angelis et al. (2002) produced several constructs able to express in vivo, in a stable fashion, large amounts of chimeric RNAs containing antisense sequences. They showed that antisense molecules against exon 51 splice junctions were able to direct skipping of that exon in the human DMD deletion 48–50 and to rescue dystrophin synthesis. They also showed that the highest skipping activity occurred when antisense constructs against the 5–prime and 3–prime splice sites were coexpressed in the same cell. The effects were tested in cultured myoblasts from a DMD patient. The deletion of exons 48–50 resulted in a premature termination codon in exon 51. The antisense sequences complementary to exon 51 splice junctions induced efficient skipping of exon 51 and partial rescue of dystrophin synthesis. X-linked dilated cardiomyopathy is a dystrophinopathy characterized by severe cardiomyopathy with no skeletal muscle involvement. Several XLCM patients have been described with mutations that abolish dystrophin muscle isoform expression, but with increased expression of brain and cerebellar Purkinje isoforms of

the gene exclusively in the skeletal muscle. Bastianutto et al. (2001) determined that 2 XLCM patients bore deletions that removed the muscle promoter and exon 1, but not the brain and cerebellar Purkinje promoters. The brain and cerebellar Purkinje promoters were found to be essentially inactive in muscle cell lines and primary cultures. Since dystrophin muscle enhancer 1 (DME1), a muscle-specific enhancer, is preserved in these patients, the authors tested its ability to upregulate the brain and cerebellar Purkinje promoters in muscle cells. Brain and cerebellar Purkinje promoter activity was significantly increased in the presence of DME1, and activation was observed exclusively in cells presenting a skeletal muscle phenotype versus cardiomyocytes. The authors suggested a role for DME1 in the induction of brain and cerebellar Purkinje isoform expression in the skeletal muscle of XLCM patients defective for muscle isoform expression. Animal model experiments lend further support to the function of DMD. Using DNA microarray, Porter et al. (2002) established a molecular signature of dystrophinopathy in the mdx mouse. In leg muscle, 242 differentially expressed genes were identified. Data provided evidence for coordinated activity of numerous compo-

nents of a chronic inflammatory response, including cytokine and chemokine signaling, leukocyte adhesion and diapedesis, invasive cell type-specific markers, and complement system activation. Upregulation of secreted phosphoprotein 1 (SPP1; 166490) mRNA and protein in dystrophic muscle identified a novel linkage between inflammatory cells and repair processes. Extracellular matrix genes were upregulated in mdx to levels similar to those in DMD. Since, unlike DMD, mdx exhibits little fibrosis, data suggested that collagen regulation at post-transcriptional stages may mediate extensive fibrosis in DMD.

[13757] It is appreciated that the abovementioned animal model for DMD is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13758] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13759] De Angelis, F. G.; Sthandier, O.; Berarducci, B.; Toso, S.; Galluzzi, G.; Ricci, E.; Cossu, G.; Bozzoni, I. : Chimeric snRNA molecules carrying antisense sequences against the splice junctions of exon 51 of the dystrophin pre-

mRNA induce exon skipping and restoration of a dystrophin synthesis in delta-48-50 DMD cells. Proc Nat. Acad. Sci. 99: 9456-9461, 2002. ; and

[13760] Bastianutto, C.; Bestard, J. A.; Lahnakoski, K.; Broere, D.; De Visser, M.; Zaccolo, M.; Pozzan, T.; Ferlini, A.; Muntoni, F.; Patarnello, T.; Klamut, H. J. : Dystrophin muscle enhance.

[13761] Further studies establishing the function and utilities of DMD are found in John Hopkins OMIM database record ID 300377, and in cited publications numbered 7833-7838, 7840, 7841-7848, 7274, 7275, 7849-7854, 4629, 7318-7323, 7276, 7324-7329, 7334-7333, 7335-7339, 7344, 7341-7343, 7277, 7351, 7353, 7354-7363, 7049, 7364-7372, 7376-7375, 7377-7378, 2930-984, 7050-7051, 98 and 988 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LAG1 Longevity Assurance Homolog 2 (*S. cerevisiae*) (LASS2, Accession XM_041889) is another VGAM218 host target gene. LASS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of LASS2 BINDING SITE, designated SEQ ID:33622, to the nucleotide sequence of VGAM218 RNA, herein designated VGAM RNA, also designated SEQ ID:2929.

[13762] Another function of VGAM218 is therefore inhibition of LAG1 Longevity Assurance Homolog 2 (*S. cerevisiae*) (LASS2, Accession XM_041889). Accordingly, utilities of VGAM218 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASS2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 219 (VGAM219) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13763] VGAM219 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM219 was detected is described hereinabove with reference to Figs. 1–8.

[13764] VGAM219 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Bovine Leukemia Virus. VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[13765] VGAM219 gene encodes a VGAM219 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM219 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM219 precursor RNA is designated SEQ ID:205, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:205 is located at position 6411 relative to the genome of Bovine Leukemia Virus.

[13766] VGAM219 precursor RNA folds onto itself, forming VGAM219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13767] An enzyme complex designated DICER COMPLEX, `dices` the VGAM219 folded precursor RNA into VGAM219 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM219 RNA is designated SEQ ID:2930, and is provided hereinbelow with reference to the sequence listing part.

[13768] VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM219 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13769] VGAM219 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM219 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM219 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13770] The complementary binding of VGAM219 RNA, herein designated VGAM RNA, to host target binding sites on VGAM219 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM219 host target RNA into VGAM219 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13771] It is appreciated that VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM219 host target genes. The mRNA of each one of this plurality of VGAM219 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM219 RNA, herein designated VGAM RNA, and which when bound by VGAM219 RNA causes inhibition of translation of respective one or more VGAM219 host target proteins.

[13772] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM219 gene, herein designated VGAM GENE, on one or more VGAM219 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13773] It is yet further appreciated that a function of VGAM219 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of viral infection by Bovine Leukemia Virus. Specific functions, and accordingly utilities, of VGAM219 correlate with, and may be deduced from, the identity of the host target genes which VGAM219 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13774] Nucleotide sequences of the VGAM219 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM219 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM219 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM219 are further described hereinbelow with reference to Table 1.

[13775] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM219 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM219 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13776] As mentioned hereinabove with reference to Fig. 1, a function of VGAM219 gene, herein designated VGAM is inhibition of expression of VGAM219 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM219 correlate with, and may be deduced from, the identity of the target genes which VGAM219 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13777] FLJ14525 (Accession NM_032800) is a VGAM219 host target gene. FLJ14525 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14525, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14525 BINDING SITE, designated SEQ ID:26547, to the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, also designated SEQ ID:2930.

[13778] A function of VGAM219 is therefore inhibition of FLJ14525 (Accession NM_032800). Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14525. KIAA1280 (Accession XM_045766) is another VGAM219 host target gene. KIAA1280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1280 BINDING SITE, designated SEQ ID:34547, to the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, also designated SEQ ID:2930.

[13779] Another function of VGAM219 is therefore inhibition of KIAA1280 (Accession XM_045766). Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1280. Vesicular Inhibitory Amino Acid Transporter (VIAAT, Accession NM_080552) is another VGAM219 host target gene. VIAAT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VIAAT, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VIAAT BINDING SITE, designated SEQ ID:27883, to the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, also designated SEQ ID:2930.

[13780] Another function of VGAM219 is therefore inhibition of Vesicular Inhibitory Amino Acid Transporter (VIAAT, Accession NM_080552). Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VIAAT. LOC197201 (Accession XM_113839) is another VGAM219 host target gene. LOC197201 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197201, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197201 BINDING SITE, designated SEQ ID:42461, to the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, also designated SEQ ID:2930.

[13781] Another function of VGAM219 is therefore inhibition of LOC197201 (Accession XM_113839). Accordingly, utilities

of VGAM219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197201. LOC221895 (Accession XM_166511) is another VGAM219 host target gene. LOC221895 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221895, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221895 BINDING SITE, designated SEQ ID:44444, to the nucleotide sequence of VGAM219 RNA, herein designated VGAM RNA, also designated SEQ ID:2930.

[13782] Another function of VGAM219 is therefore inhibition of LOC221895 (Accession XM_166511). Accordingly, utilities of VGAM219 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221895. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 220 (VGAM220) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13783] VGAM220 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM220 was detected is described hereinabove with reference to Figs. 1–8.

[13784] VGAM220 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13785] VGAM220 gene encodes a VGAM220 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM220 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM220 precursor RNA is designated SEQ ID:206, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:206 is located at position 16550 relative to the genome of Callitrichine Herpesvirus 3.

[13786] VGAM220 precursor RNA folds onto itself, forming VGAM220 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13787] An enzyme complex designated DICER COMPLEX, `dices` the VGAM220 folded precursor RNA into VGAM220 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM220 RNA is designated SEQ ID:2931, and is provided hereinbelow with reference to the sequence listing part.

[13788] VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM220 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[13789] VGAM220 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM220 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM220 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13790] The complementary binding of VGAM220 RNA, herein designated VGAM RNA, to host target binding sites on VGAM220 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM220 host target RNA into VGAM220 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13791] It is appreciated that VGAM220 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM220 host target genes. The mRNA of each one of this plurality of VGAM220 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM220 RNA, herein designated VGAM RNA, and which when bound by VGAM220 RNA causes inhibition of translation of respective one or more VGAM220 host target proteins.

[13792] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM220 gene, herein designated VGAM GENE, on one or more VGAM220 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13793] It is yet further appreciated that a function of VGAM220 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of viral infection by Callicitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM220 correlate with, and may be deduced from, the identity of the host target genes which VGAM220 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13794] Nucleotide sequences of the VGAM220 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM220 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM220 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM220 are further
described hereinbelow with reference to Table 1.

[13795] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM220 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM220 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[13796] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM220 gene, herein designated VGAM is
inhibition of expression of VGAM220 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM220 correlate with, and may be deduced
from, the identity of the target genes which VGAM220
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[13797] B-cell CLL/lymphoma 7A (BCL7A, Accession NM_020993)
is a VGAM220 host target gene. BCL7A BINDING SITE is

HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BCL7A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL7A BINDING SITE, designated SEQ ID:21989, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13798] A function of VGAM220 is therefore inhibition of B-cell CLL/lymphoma 7A (BCL7A, Accession NM_020993). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL7A. Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM_053056) is another VGAM220 host target gene. CCND1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND1 BINDING SITE, designated SEQ ID:27598, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13799] Another function of VGAM220 is therefore inhibition of Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM_053056), a gene which is involved in the control of cell cycle and is required for Schwann cell proliferation to proceed normally during Wallerian degeneration. Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND1. The function of CCND1 has been established by previous studies. Tsujimoto et al. (1984) cloned the chromosomal breakpoint of chronic lymphocytic leukemia (CLL; OMIM Ref. No. 151400) cells of the B-cell type carrying t(11;14)(q13;q32). The breakpoint was in the joining segment of the heavy chain locus on chromosome 14. A probe that is specific for chromosome 11 and maps immediately 5-prime to the breakpoint on 14q+ was isolated. The probe detected a rearrangement of the homologous genomic DNA segment in CLL cells and in DNA from a diffuse large cell lymphoma with the t(11;14) translocation. This rearranged DNA segment was not present in Burkitt lymphoma cells with the t(8;14) translocation or in nonneoplastic human lymphoblastoid cells. The probe thus can be used to identify and characterize a gene located on 11q13 involved in the

malignant transformation of B cells in the t(11;14) translocation. Tsujimoto et al. (1984) referred to this gene as BCL1. In 2 different cases of B-cell chronic lymphatic leukemia, Tsujimoto et al. (1985) found that the breakpoints on chromosome 11 were within 8 nucleotides of each other and on chromosome 14 involved the J4 DNA segment of the Ig heavy chain segment. Because they detected a 7mer–9mer signallike sequence with a 12–base–long spacer on the normal chromosome 11, close to the breakpoint, they speculated that the t(11;14) chromosome translocation in CLL may be sequence specific and may involve the recombination system for immunoglobulin V–D–J gene segment joining. Animal model experiments lend further support to the function of CCND1. Ma et al. (1998) studied cyclin D1–deficient mice, which have small eyes with thin retinas, and observed that there was a lower level of retinal cell proliferation and a unique pattern of photoreceptor cell death. Death was first observed in scattered clusters of cells in the retina. It then appeared to spread from these few cells to nearby photoreceptors, eventually producing extensive holes in the photoreceptor layer. These holes appeared to be filled with interneurons from the inner nuclear layer. The death

occurred mainly during the second to fourth postnatal weeks. Other models of photoreceptor degeneration in rodents differed in that they occur more uniformly across the retina, with death proceeding over a longer period of time until all, or nearly all, of the photoreceptors degenerate. Ma et al. (1998) found that expression of a bcl2 transgene could not prevent the death.

[13800] It is appreciated that the abovementioned animal model for CCND1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[13801] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13802] Ma, C.; Papermaster, D.; Cepko, C. L. : A unique pattern of photoreceptor degeneration in cyclin D1 mutant mice. Proc. Nat. Acad. Sci. 95: 9938–9943, 1998. ; and

[13803] Tsujimoto, Y.; Yunis, J.; Onorato–Showe, L.; Erikson, J.; Nowell, P. C.; Croce, C. M. : Molecular cloning of the chromosomal breakpoint of B–cell lymphomas and leukemias with the t(11;1.

[13804] Further studies establishing the function and utilities of CCND1 are found in John Hopkins OMIM database record

ID 168461, and in cited publications numbered 2389, 4458, 5452–5453, 11374, 5455–5456, 5468–4344, 5470–5479, 11078–5481, 5614, 11079–1108 and 5615–5618 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chediak–Higashi Syndrome 1 (CHS1, Accession NM_000081) is another VGAM220 host target gene. CHS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHS1 BINDING SITE, designated SEQ ID:5524, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13805] Another function of VGAM220 is therefore inhibition of Chediak–Higashi Syndrome 1 (CHS1, Accession NM_000081), a gene which may sort endosomal resident proteins into late multivesicular endosome. Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHS1. The function of CHS1 and its association with various diseases and clinical conditions, has been estab-

lished by previous studies, as described hereinabove with reference to VGAM191. Eukaryotic Translation Initiation Factor 2B, Subunit 1 Alpha, 26kDa (EIF2B1, Accession XM_006566) is another VGAM220 host target gene.

EIF2B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2B1 BINDING SITE, designated SEQ ID:30004, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13806] Another function of VGAM220 is therefore inhibition of Eukaryotic Translation Initiation Factor 2B, Subunit 1 Alpha, 26kDa (EIF2B1, Accession XM_006566). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF2B1. Molybdenum Cofactor Synthesis 2 (MOCS2, Accession NM_004531) is another VGAM220 host target gene. MOCS2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MOCS2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MOCS2 BINDING SITE, designated SEQ ID:10873, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13807] Another function of VGAM220 is therefore inhibition of Molybdenum Cofactor Synthesis 2 (MOCS2, Accession NM_004531). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MOCS2. Mature T-cell Proliferation 1 (MTCP1, Accession NM_014221) is another VGAM220 host target gene. MTCP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MTCP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTCP1 BINDING SITE, designated SEQ ID:15483, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13808] Another function of VGAM220 is therefore inhibition of Mature T-cell Proliferation 1 (MTCP1, Accession

NM_014221). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTCP1. N4BP2 (Accession NM_018177) is another VGAM220 host target gene.

N4BP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by N4BP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP2 BINDING SITE, designated SEQ ID:20003, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13809] Another function of VGAM220 is therefore inhibition of N4BP2 (Accession NM_018177). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP2. RALGPS1A (Accession NM_014636) is another VGAM220 host target gene. RALGPS1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RALGPS1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of RALGPS1A BINDING SITE, designated SEQ ID:16016, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13810] Another function of VGAM220 is therefore inhibition of RALGPS1A (Accession NM_014636). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RALGPS1A. LOC144348 (Accession XM_084826) is another VGAM220 host target gene. LOC144348 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144348, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144348 BINDING SITE, designated SEQ ID:37720, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13811] Another function of VGAM220 is therefore inhibition of LOC144348 (Accession XM_084826). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144348. LOC196418 (Accession XM_113717) is an-

other VGAM220 host target gene. LOC196418 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196418 BINDING SITE, designated SEQ ID:42368, to the nucleotide sequence of VGAM220 RNA, herein designated VGAM RNA, also designated SEQ ID:2931.

[13812] Another function of VGAM220 is therefore inhibition of LOC196418 (Accession XM_113717). Accordingly, utilities of VGAM220 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196418. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 221 (VGAM221) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13813] VGAM221 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM221 was detected is described

hereinabove with reference to Figs. 1–8.

[13814] VGAM221 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13815] VGAM221 gene encodes a VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM221 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM221 precursor RNA is designated SEQ ID:207, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:207 is located at position 46723 relative to the genome of Callitrichine Herpesvirus 3.

[13816] VGAM221 precursor RNA folds onto itself, forming VGAM221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13817] An enzyme complex designated DICER COMPLEX, `dices` the VGAM221 folded precursor RNA into VGAM221 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM221 RNA is designated SEQ ID:2932, and is provided hereinbelow with reference to the sequence listing part.

[13818] VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM221 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13819] VGAM221 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM221 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM221 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM221 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13820] The complementary binding of VGAM221 RNA, herein designated VGAM RNA, to host target binding sites on VGAM221 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM221 host target RNA into VGAM221 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13821] It is appreciated that VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM221 host target genes. The mRNA of each one of this plurality of VGAM221 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM221 RNA, herein designated VGAM RNA, and which when bound by VGAM221 RNA causes inhibition of translation of respective one or more VGAM221 host target proteins.

[13822] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM221 gene, herein designated VGAM GENE, on one or more VGAM221 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13823] It is yet further appreciated that a function of VGAM221 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM221 correlate with, and may be deduced from, the identity of the host target genes which VGAM221 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13824] Nucleotide sequences of the VGAM221 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM221 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM221 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM221 are further described hereinbelow with reference to Table 1.

[13825] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM221 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM221 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13826] As mentioned hereinabove with reference to Fig. 1, a function of VGAM221 gene, herein designated VGAM is inhibition of expression of VGAM221 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM221 correlate with, and may be deduced from, the identity of the target genes which VGAM221 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13827] Breast Carcinoma Amplified Sequence 1 (BCAS1, Accession NM_003657) is a VGAM221 host target gene. BCAS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCAS1, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCAS1 BINDING SITE, designated SEQ ID:9730, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13828] A function of VGAM221 is therefore inhibition of Breast Carcinoma Amplified Sequence 1 (BCAS1, Accession NM_003657). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCAS1. Cysteine Knot Superfamily 1, BMP Antagonist 1 (CKTSF1B1, Accession NM_013372) is another VGAM221 host target gene. CKTSF1B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CKTSF1B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CKTSF1B1 BINDING SITE, designated SEQ ID:15026, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13829] Another function of VGAM221 is therefore inhibition of Cysteine Knot Superfamily 1, BMP Antagonist 1

(CKTSF1B1, Accession NM_013372), a gene which blocks signaling of bone morphogenetic protein (BMP) . Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CKTSF1B1. The function of CKTSF1B1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28.CTP Synthase (CTPS, Accession XM_114141) is another VGAM221 host target gene. CTPS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTPS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTPS BINDING SITE, designated SEQ ID:42714, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13830] Another function of VGAM221 is therefore inhibition of CTP Synthase (CTPS, Accession XM_114141), a gene which is important in the biosynthesis of phospholipids and nucleic acids. Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTPS. The function of CTPS has

been established by previous studies. The catalytic conversion of UTP to CTP is accomplished by the enzyme cytidine-5-prime-triphosphate synthetase (UTP:L-glutamine amido ligase; EC 6.3.4.2). The enzyme is important in the biosynthesis of phospholipids and nucleic acids, and plays a key role in cell growth, development, and tumorigenesis. Thomas et al. (1989) isolated a cDNA clone of the CTP synthetase gene from a rat liver cDNA library. It is a key regulatory enzyme in pyrimidine biosynthesis. These authors have isolated both cDNA and genomic gene sequences from the rat and Chinese hamster. Yamauchi et al. (1990) cloned the CTPS gene and showed that the open reading frame encodes 591 amino acids that have a striking degree of similarity to the structural gene in *E. coli*. Yamauchi et al. (1991) assigned the structural gene to 1p by study of a panel of human/rodent somatic cell hybrids and the CTPS cDNA. By a method of mapping that combines fluorescence in situ hybridization with replicated prometaphase R-bands (Takahashi et al., 1990), Takahashi et al. (1991) mapped the CTPS gene to 1p34.3-p34.1. By high-resolution banding analysis, they further narrowed the assignment to 1p34.1; see Yamauchi et al. (1991). The genomic sequence is distributed in 19

exons covering about 35 kb. Mutations eliminating the feedback regulation of CTPS result in multidrug resistance and mutator phenotype in Chinese hamster ovary (CHO) cells. The region to which the CTPS gene has been mapped is the location of breakpoints involved in several tumor types. Yamauchi et al. (1993) found that inactivating mutations clustered in a highly conserved region of the gene make it feasible to assess the role of such mutations in the development of drug resistance encountered in the treatment of malignant disease and not readily explained by altered expression of the multidrug resistance genes (e.g., 171050).

[13831] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13832] Yamauchi, M.; Yamauchi, N.; Phear, G.; Spurr, N. K.; Martinsson, T.; Weith, A.; Meuth, M. : Genomic organization and chromosomal localization of the human CTP synthetase gene (CTPS). *Genomics* 11: 1088–1096, 1991. ; and

[13833] Whelan, J.; Phear, G.; Yamauchi, M.; Meuth, M. : Clustered base substitutions in CTP synthetase conferring drug resistance in Chinese hamster ovary cells. *Nature Genet.* 3:

317-322, 1993.

[13834] Further studies establishing the function and utilities of CTPS are found in John Hopkins OMIM database record ID 123860, and in cited publications numbered 12754-12759, and 3981 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epithelial Cell Transforming Sequence 2 Oncogene (ECT2, Accession NM_018098) is another VGAM221 host target gene. ECT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ECT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ECT2 BINDING SITE, designated SEQ ID:19871, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13835] Another function of VGAM221 is therefore inhibition of Epithelial Cell Transforming Sequence 2 Oncogene (ECT2, Accession NM_018098), a gene which is a transforming protein that can interact with Rho-like proteins of the Ras superfamily. Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with ECT2. The function of ECT2 has been established by previous studies. ECT2 is a transforming protein that can interact with Rho-like proteins of the Ras superfamily. First isolated in the mouse, the Ect2 gene acts as an oncogene. To investigate its involvement in human tumors, Takai et al. (1995) isolated the human homolog, ECT2, and by fluorescence in situ hybridization determined that the gene is located on 3q26.1–q26.2. Localization to chromosome 3 was confirmed by PCR analysis of human/hamster somatic cell hybrid DNAs. Takai et al. (1998) mapped the Ect2 gene to mouse chromosome band 3B by in situ hybridization. They commented that the EVI1 (OMIM Ref. No. 165215) and Fim3 genes (OMIM Ref. No. 136770) are also in mouse 3B and that the human counterparts of these genes are also linked to ECT2, indicating that this chromosome region is evolutionarily conserved between human and mouse.

[13836] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13837] Takai, S.; Long, J. E.; Yamada, K.; Miki, T. : Chromosomal localization of the human ECT2 proto-oncogene to 3q26.1–q26.2 by somatic cell analysis and fluorescence in

situ hybridization. Genomics 27: 220–222, 1995. ; and

[13838] Takai, S.; Lorenzi, M. V.; Long, J. E.; Yamada, K.; Miki, T. : Assignment of the Ect2 protooncogene to mouse chromosome band 3B by in situ hybridization. Cytogenet. Cell Genet. 81: 83–84.

[13839] Further studies establishing the function and utilities of ECT2 are found in John Hopkins OMIM database record ID 600586, and in cited publications numbered 10215–10216 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Hematopoietic Protein 1 (HEM1, Accession NM_005337) is another VGAM221 host target gene. HEM1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HEM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEM1 BINDING SITE, designated SEQ ID:11808, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13840] Another function of VGAM221 is therefore inhibition of Hematopoietic Protein 1 (HEM1, Accession NM_005337). Accordingly, utilities of VGAM221 include diagnosis, pre-

vention and treatment of diseases and clinical conditions associated with HEM1. Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242) is another VGAM221 host target gene. TGFB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB2 BINDING SITE, designated SEQ ID:9244, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13841] Another function of VGAM221 is therefore inhibition of Transforming Growth Factor, Beta Receptor II (70/80kDa) (TGFB2, Accession NM_003242). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFB2. DKFZP564D0478 (Accession NM_032125) is another VGAM221 host target gene. DKFZP564D0478 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D0478, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of DKFZP564D0478 BINDING SITE, designated SEQ ID:25809, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13842] Another function of VGAM221 is therefore inhibition of DKFZP564D0478 (Accession NM_032125). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D0478. FLJ22169 (Accession NM_024085) is another VGAM221 host target gene. FLJ22169 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22169, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22169 BINDING SITE, designated SEQ ID:23519, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13843] Another function of VGAM221 is therefore inhibition of FLJ22169 (Accession NM_024085). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22169.

KIAA0205 (Accession NM_014873) is another VGAM221 host target gene. KIAA0205 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0205, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0205 BINDING SITE, designated SEQ ID:17005, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13844] Another function of VGAM221 is therefore inhibition of KIAA0205 (Accession NM_014873). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0205. KIAA0685 (Accession NM_014678) is another VGAM221 host target gene. KIAA0685 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0685, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0685 BINDING SITE, designated SEQ ID:16149, to the nucleotide sequence of VGAM221 RNA, herein designated

VGAM RNA, also designated SEQ ID:2932.

[13845] Another function of VGAM221 is therefore inhibition of KIAA0685 (Accession NM_014678). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0685. LOC196283 (Accession XM_113684) is another VGAM221 host target gene. LOC196283 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196283, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196283 BINDING SITE, designated SEQ ID:42339, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13846] Another function of VGAM221 is therefore inhibition of LOC196283 (Accession XM_113684). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196283. LOC203248 (Accession XM_114659) is another VGAM221 host target gene. LOC203248 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203248, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203248 BINDING SITE, designated SEQ ID:43017, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13847] Another function of VGAM221 is therefore inhibition of LOC203248 (Accession XM_114659). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203248. LOC219731 (Accession XM_167596) is another VGAM221 host target gene. LOC219731 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219731, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219731 BINDING SITE, designated SEQ ID:44717, to the nucleotide sequence of VGAM221 RNA, herein designated VGAM RNA, also designated SEQ ID:2932.

[13848] Another function of VGAM221 is therefore inhibition of LOC219731 (Accession XM_167596). Accordingly, utilities of VGAM221 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC219731. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 222 (VGAM222) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13849] VGAM222 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM222 was detected is described hereinabove with reference to Figs. 1–8.

[13850] VGAM222 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13851] VGAM222 gene encodes a VGAM222 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM222 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM222 precursor RNA is designated SEQ

ID:208, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:208 is located at position 94113 relative to the genome of Calitrichine Herpesvirus 3.

[13852] VGAM222 precursor RNA folds onto itself, forming VGAM222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13853] An enzyme complex designated DICER COMPLEX, `dices` the VGAM222 folded precursor RNA into VGAM222 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM222 RNA is designated SEQ ID:2933, and is provided hereinbelow with reference to the sequence

listing part.

[13854] VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM222 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13855] VGAM222 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM222 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM222 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13856] The complementary binding of VGAM222 RNA, herein designated VGAM RNA, to host target binding sites on VGAM222 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM222 host target RNA into VGAM222 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13857] It is appreciated that VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM222 host target genes. The mRNA of each one of this plurality of VGAM222 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM222 RNA, herein designated VGAM

RNA, and which when bound by VGAM222 RNA causes inhibition of translation of respective one or more VGAM222 host target proteins.

[13858] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM222 gene, herein designated VGAM GENE, on one or more VGAM222 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13859] It is yet further appreciated that a function of VGAM222 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM222 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM222 correlate with, and may be deduced from, the identity of the host target genes which VGAM222 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13860] Nucleotide sequences of the VGAM222 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM222 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM222 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM222 are further described hereinbelow with reference to Table 1.

[13861] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM222 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM222 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13862] As mentioned hereinabove with reference to Fig. 1, a function of VGAM222 gene, herein designated VGAM is

inhibition of expression of VGAM222 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM222 correlate with, and may be deduced from, the identity of the target genes which VGAM222 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13863] SAR1 (Accession NM_020150) is a VGAM222 host target gene. SAR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SAR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SAR1 BINDING SITE, designated SEQ ID:21350, to the nucleotide sequence of VGAM222 RNA, herein designated VGAM RNA, also designated SEQ ID:2933.

[13864] A function of VGAM222 is therefore inhibition of SAR1 (Accession NM_020150), a gene which is involved in transport from the endoplasmic reticulum to the golgi apparatus (by similarity). Accordingly, utilities of VGAM222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SAR1. The function of SAR1 has been established by previous studies. Sugimoto et al. (2001) demonstrated that IQGAP1, a negative

regulator of cell–cell adhesion, is upregulated by gene amplification at 15q26 in 2 gastric cancer cell lines. Amplification at 15q26 had been found in various malignancies, including breast cancers, and FES (OMIM Ref. No. 190030) and/or IGF1R (OMIM Ref. No. 147370) had been identified as targets for gene amplification in breast cancer, melanoma, and pancreatic adenocarcinoma. In contrast, Sugimoto et al. (2001) found that both genes are located telomeric to the amplicon at 15q26 in the 2 gastric cancer cell lines they studied. Fukata et al. (2002) found that IQGAP1, an effector of RAC1 (OMIM Ref. No. 602048) and CDC42, interacts with CLIP170 (RSN; 179838). In Vero fibroblasts, IQGAP1 localized at the polarized leading edge. Expression of a C–terminal fragment of IQGAP1 that included the CLIP170–binding region delocalized GFP–CLIP170 from the tips of microtubules and altered the microtubule array. The authors found that activated RAC1/CDC42, IQGAP1, and CLIP170 form a tripartite complex. Furthermore, expression of an IQGAP1 mutant defective in RAC1/CDC42 binding induced multiple leading edges. These results indicated that RAC1/CDC42 marks special cortical spots where the IQGAP1 and CLIP170 complex is targeted, leading to a polarized mi–

crotubule array and cell polarization.

[13865] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13866] Sugimoto, N.; Imoto, I.; Fukuda, Y.; Kurihara, N.; Kuroda, S.; Tanigami, A.; Kaibuchi, K.; Kamiyama, R.; Inazawa, J. : IQGAP1, a negative regulator of cell–cell adhesion, is up–regulated by gene amplification at 15q26 in gastric cancer cell lines HSC39 and 40A. J. Hum. Genet. 46: 21–25, 2001. ; and

[13867] Fukata, M.; Watanabe, T.; Noritake, J.; Nakagawa, M.; Yamaga, M.; Kuroda, S.; Matsuura, Y.; Iwamatsu, A.; Perez, F.; Kaibuchi, K. : Rac1 and Cdc42 capture microtubules through IQGAP1 an.

[13868] Further studies establishing the function and utilities of SAR1 are found in John Hopkins OMIM database record ID 603379, and in cited publications numbered 180 and 7498–7500 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 4 (SLC4A4, Accession NM_003759) is another VGAM222 host target gene. SLC4A4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by SLC4A4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC4A4 BINDING SITE, designated SEQ ID:9835, to the nucleotide sequence of VGAM222 RNA, herein designated VGAM RNA, also designated SEQ ID:2933.

[13869] Another function of VGAM222 is therefore inhibition of Solute Carrier Family 4, Sodium Bicarbonate Cotransporter, Member 4 (SLC4A4, Accession NM_003759), a gene which is a sodium bicarbonate cotransporter. Accordingly, utilities of VGAM222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC4A4. The function of SLC4A4 has been established by previous studies. By screening a human heart cDNA library with rat kidney Nbc cDNAs, followed by a PCR approach, Choi et al. (1999) isolated a full-length cDNA encoding a heart NBC, which they called hhNBC. They reported that the coding sequence of hhNBC is identical to that of pNBC (Abuladze et al., 1998). However, the 5-prime untranslated regions of hhNBC and pNBC differ. Northern blot analysis using the 5-prime region of the hhNBC coding sequence as probe detected an approxi-

mately 9-kb transcript that was strongly expressed in pancreas and weakly expressed in heart and brain. Choi et al. (1999) found that both hhNBC and kNBC (Burnham et al., 1997), when expressed in *Xenopus*, are electrogenic. Soleimani and Burnham (2000) stated that kNBC (Burnham et al., 1997) and pNBC (Abuladze et al., 1998) are encoded by splice variants of the same gene, SLC4A4, which they called NBC1. Mutations in the SLC4A4 gene (e.g., 603345.0001, 603345.0002) cause proximal renal tubular acidosis with bilateral glaucoma, cataracts, and band keratopathy (OMIM Ref. No. 604278). Such mutations may increase the bicarbonate concentration in the corneal stroma, which would facilitate calcium deposition leading to band keratopathy. Igarashi et al. (1999) suggested that the kidney and pancreatic NBCs are derived from a common gene by alternative splicing and that mutations at the common region would inactivate both isoforms. Studies by Usui et al. (1999) confirmed that both kidney and pancreatic NBC are involved in the transport of sodium and bicarbonate out of the corneal stroma and into the aqueous humor.

[13870] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [13871] Soleimani, M.; Burnham, C. E. : Physiologic and molecular aspects of the Na(+):HCO(3-) cotransporter in health and disease processes. *Kidney Int.* 57: 371–384, 2000. ; and
- [13872] Choi, I.; Romero, M. F.; Khandoudi, N.; Bril, A.; Boron, W. F. : Cloning and characterization of a human electrogenic Na(+)-HCO(3-) cotransporter isoform (hhNBC). *Am. J. Physiol.* 276: C57.
- [13873] Further studies establishing the function and utilities of SLC4A4 are found in John Hopkins OMIM database record ID 603345, and in cited publications numbered 7954–7960 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Factor Dp-2 (E2F dimerization partner 2) (TFDP2, Accession NM_006286) is another VGAM222 host target gene. TFDP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TFDP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TFDP2 BINDING SITE, designated SEQ ID:12972, to the nucleotide sequence of VGAM222 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2933.

[13874] Another function of VGAM222 is therefore inhibition of Transcription Factor Dp-2 (E2F dimerization partner 2) (TFDP2, Accession NM_006286), a gene which is required for the progression of S-phase during the cell cycle. Accordingly, utilities of VGAM222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TFDP2. The function of TFDP2 has been established by previous studies. Zhang and Chellappan (1995) cloned an E2F dimerization partner, transcription factor DP2, from a human kidney cDNA library. The TFDP2 gene encodes a predicted 386-amino acid protein that is 68% identical to TFDP1 (OMIM Ref. No. 189902). Northern blot analysis revealed 5 distinct transcript sizes ranging from 1.4 to 9.5 kb, with expression of at least one size observed in all cell lines tested. TFDP2 is able to form a functional heterodimer with E2F1 (OMIM Ref. No. 189971). Zhang et al. (1997) used fluorescence in situ hybridization to map the TFDP2 gene to human chromosome 3q23.

[13875] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13876] Zhang, Y.; Chellappan, S. P. : Cloning and characterization

of human DP2, a novel dimerization partner of E2F. *Oncogene* 10: 2085–2093, 1995. ; and

[13877] Zhang, Y.; Venkatraj, V. S.; Fischer, S. G.; Warburton, D.; Chellappan, S. P. : Genomic cloning and chromosomal assignment of the E2F dimerization partner TFDP gene family. *Genomics* 39:.

[13878] Further studies establishing the function and utilities of TFDP2 are found in John Hopkins OMIM database record ID 602160, and in cited publications numbered 76 and 12350 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0923 (Accession NM_014021) is another VGAM222 host target gene. KIAA0923 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0923, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0923 BINDING SITE, designated SEQ ID:15238, to the nucleotide sequence of VGAM222 RNA, herein designated VGAM RNA, also designated SEQ ID:2933.

[13879] Another function of VGAM222 is therefore inhibition of KIAA0923 (Accession NM_014021). Accordingly, utilities

of VGAM222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0923. Zinc Finger Protein 238 (ZNF238, Accession NM_006352) is another VGAM222 host target gene. ZNF238 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF238, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF238 BINDING SITE, designated SEQ ID:13042, to the nucleotide sequence of VGAM222 RNA, herein designated VGAM RNA, also designated SEQ ID:2933.

[13880] Another function of VGAM222 is therefore inhibition of Zinc Finger Protein 238 (ZNF238, Accession NM_006352). Accordingly, utilities of VGAM222 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF238. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 223 (VGAM223) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target

genes is known in the art.

[13881] VGAM223 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM223 was detected is described hereinabove with reference to Figs. 1–8.

[13882] VGAM223 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13883] VGAM223 gene encodes a VGAM223 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM223 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM223 precursor RNA is designated SEQ ID:209, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:209 is located at position 133004 relative to the genome of Callitrichine Herpesvirus 3.

[13884] VGAM223 precursor RNA folds onto itself, forming VGAM223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[13885] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM223 folded precursor RNA into VGAM223 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 44%) nucleotide se-
quence of VGAM223 RNA is designated SEQ ID:2934, and
is provided hereinbelow with reference to the sequence
listing part.

[13886] VGAM223 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM223 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM223 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[13887] VGAM223 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM223 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM223 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[13888] The complementary binding of VGAM223 RNA, herein designated VGAM RNA, to host target binding sites on VGAM223 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM223 host target RNA into VGAM223 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13889] It is appreciated that VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM223 host target genes. The mRNA of each one of this plurality of VGAM223 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM223 RNA, herein designated VGAM RNA, and which when bound by VGAM223 RNA causes inhibition of translation of respective one or more VGAM223 host target proteins.

[13890] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM223 gene, herein designated VGAM GENE, on one or

more VGAM223 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13891] It is yet further appreciated that a function of VGAM223 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM223 correlate with, and may be deduced from, the identity of the host target genes which VGAM223 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [13892] Nucleotide sequences of the VGAM223 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM223 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM223 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM223 are further described hereinbelow with reference to Table 1.
- [13893] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM223 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM223 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [13894] As mentioned hereinabove with reference to Fig. 1, a function of VGAM223 gene, herein designated VGAM is inhibition of expression of VGAM223 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM223 correlate with, and may be deduced from, the identity of the target genes which VGAM223 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [13895] Dual Specificity Phosphatase 4 (DUSP4, Accession

NM_001394) is a VGAM223 host target gene. DUSP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DUSP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP4 BINDING SITE, designated SEQ ID:7090, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13896] A function of VGAM223 is therefore inhibition of Dual Specificity Phosphatase 4 (DUSP4, Accession NM_001394), a gene which regulates mitogenic signal transduction. Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP4. The function of DUSP4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM110. Niemann-Pick Disease, Type C1 (NPC1, Accession NM_000271) is another VGAM223 host target gene. NPC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPC1 BINDING SITE, designated SEQ ID:5815, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13897] Another function of VGAM223 is therefore inhibition of Niemann–Pick Disease, Type C1 (NPC1, Accession NM_000271). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPC1. Transcription Factor–like 4 (TCFL4, Accession XM_032817) is another VGAM223 host target gene. TCFL4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TCFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCFL4 BINDING SITE, designated SEQ ID:31770, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13898] Another function of VGAM223 is therefore inhibition of Transcription Factor–like 4 (TCFL4, Accession XM_032817), a gene which interacts with Mad and re–

presses transcription by recruiting the Sin3A–histone deacetylase corepressor complex. Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL4. The function of TCFL4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Zinc Finger Protein (C2H2 type) 277 (ZNF277, Accession NM_021994) is another VGAM223 host target gene. ZNF277 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF277, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF277 BINDING SITE, designated SEQ ID:22535, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13899] Another function of VGAM223 is therefore inhibition of Zinc Finger Protein (C2H2 type) 277 (ZNF277, Accession NM_021994). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF277. Chromosome 11

Open Reading Frame 9 (C11orf9, Accession NM_013279) is another VGAM223 host target gene. C11orf9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf9 BINDING SITE, designated SEQ ID:14946, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13900] Another function of VGAM223 is therefore inhibition of Chromosome 11 Open Reading Frame 9 (C11orf9, Accession NM_013279). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf9. DKFZP564I0422 (Accession NM_031435) is another VGAM223 host target gene. DKFZP564I0422 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564I0422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564I0422 BINDING SITE, designated SEQ ID:25435, to

the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13901] Another function of VGAM223 is therefore inhibition of DKFZP564I0422 (Accession NM_031435). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564I0422. FLJ12076 (Accession NM_025187) is another VGAM223 host target gene. FLJ12076 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12076, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12076 BINDING SITE, designated SEQ ID:24825, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13902] Another function of VGAM223 is therefore inhibition of FLJ12076 (Accession NM_025187). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12076. FLJ22596 (Accession NM_025086) is another VGAM223 host target gene. FLJ22596 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA

encoded by FLJ22596, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22596 BINDING SITE, designated SEQ ID:24705, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13903] Another function of VGAM223 is therefore inhibition of FLJ22596 (Accession NM_025086). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22596. HA-1 (Accession XM_037574) is another VGAM223 host target gene. HA-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HA-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HA-1 BINDING SITE, designated SEQ ID:32654, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13904] Another function of VGAM223 is therefore inhibition of HA-1 (Accession XM_037574). Accordingly, utilities of

VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HA-1.

KIAA1056 (Accession NM_014894) is another VGAM223 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17048, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13905] Another function of VGAM223 is therefore inhibition of KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. KIAA1193 (Accession XM_041843) is another VGAM223 host target gene. KIAA1193 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1193 BINDING SITE, designated SEQ ID:33607, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13906] Another function of VGAM223 is therefore inhibition of KIAA1193 (Accession XM_041843). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1193. KIAA1753 (Accession XM_036115) is another VGAM223 host target gene. KIAA1753 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1753, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1753 BINDING SITE, designated SEQ ID:32380, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13907] Another function of VGAM223 is therefore inhibition of KIAA1753 (Accession XM_036115). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1753. Protocadherin 10 (PCDH10, Accession NM_020815) is another VGAM223 host target gene.

PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDH10, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDH10 BINDING SITE1 and PCDH10 BINDING SITE2, designated SEQ ID:21882 and SEQ ID:26767 respectively, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13908] Another function of VGAM223 is therefore inhibition of Protocadherin 10 (PCDH10, Accession NM_020815). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDH10. LOC203377 (Accession XM_117540) is another VGAM223 host target gene. LOC203377 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203377, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203377 BINDING SITE, designated SEQ ID:43543, to the nucleotide sequence of

VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13909] Another function of VGAM223 is therefore inhibition of LOC203377 (Accession XM_117540). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203377. LOC219654 (Accession XM_166095) is another VGAM223 host target gene. LOC219654 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219654, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219654 BINDING SITE, designated SEQ ID:43879, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13910] Another function of VGAM223 is therefore inhibition of LOC219654 (Accession XM_166095). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219654. LOC220070 (Accession NM_145308) is another VGAM223 host target gene. LOC220070 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC220070, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220070 BINDING SITE, designated SEQ ID:29819, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13911] Another function of VGAM223 is therefore inhibition of LOC220070 (Accession NM_145308). Accordingly, utilities of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220070. LOC56959 (Accession XM_088578) is another VGAM223 host target gene. LOC56959 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56959, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56959 BINDING SITE, designated SEQ ID:39839, to the nucleotide sequence of VGAM223 RNA, herein designated VGAM RNA, also designated SEQ ID:2934.

[13912] Another function of VGAM223 is therefore inhibition of LOC56959 (Accession XM_088578). Accordingly, utilities

of VGAM223 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56959. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 224 (VGAM224) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13913] VGAM224 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM224 was detected is described hereinabove with reference to Figs. 1–8.

[13914] VGAM224 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13915] VGAM224 gene encodes a VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM224 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM224 precursor RNA is designated SEQ ID:210, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:210 is located at position 52378 relative to the genome of Calitrichine Herpesvirus 3.

[13916] VGAM224 precursor RNA folds onto itself, forming VGAM224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13917] An enzyme complex designated DICER COMPLEX, `dices` the VGAM224 folded precursor RNA into VGAM224 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM224 RNA is designated SEQ ID:2935, and

is provided hereinbelow with reference to the sequence listing part.

[13918] VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM224 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13919] VGAM224 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM224 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM224 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13920] The complementary binding of VGAM224 RNA, herein designated VGAM RNA, to host target binding sites on VGAM224 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM224 host target RNA into VGAM224 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13921] It is appreciated that VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM224 host target genes. The mRNA of each one of this plurality of VGAM224 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM224 RNA, herein designated VGAM RNA, and which when bound by VGAM224 RNA causes inhibition of translation of respective one or more VGAM224 host target proteins.

[13922] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM224 gene, herein designated VGAM GENE, on one or more VGAM224 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13923] It is yet further appreciated that a function of VGAM224 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM224 correlate with, and may be deduced from, the identity of the host target genes which VGAM224 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13924] Nucleotide sequences of the VGAM224 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM224 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM224 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM224 are further described hereinbelow with reference to Table 1.

[13925] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM224 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM224 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13926] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM224 gene, herein designated VGAM is inhibition of expression of VGAM224 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM224 correlate with, and may be deduced from, the identity of the target genes which VGAM224 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13927] Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774) is a VGAM224 host target gene. ANK1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANK1 BINDING SITE, designated SEQ ID:30287, to the nucleotide sequence of VGAM224 RNA, herein designated VGAM RNA, also designated SEQ ID:2935.

[13928] A function of VGAM224 is therefore inhibition of Ankyrin 1, Erythrocytic (ANK1, Accession XM_016774). Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANK1. Fer (fps/fes related) Tyrosine Kinase (phosphoprotein NCP94) (FER, Accession NM_005246) is

another VGAM224 host target gene. FER BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FER, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FER BINDING SITE, designated SEQ ID:11755, to the nucleotide sequence of VGAM224 RNA, herein designated VGAM RNA, also designated SEQ ID:2935.

[13929] Another function of VGAM224 is therefore inhibition of Fer (fps/fes related) Tyrosine Kinase (phosphoprotein NCP94) (FER, Accession NM_005246), a gene which Non-receptor protein tyrosine kinase; member of the Src family. Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FER. The function of FER has been established by previous studies. To identify novel protein tyrosine kinase genes expressed in human lymphoid cells, Krolewski et al. (1990) screened B- and T-cell cDNA libraries at low stringency using an FMS (OMIM Ref. No. 164770) tyrosine kinase domain probe. One of 3 genes so identified had been cloned previously by Hao et al. (1989). Arregui et al. (2000) demonstrated that cell-permeable

(OMIM Ref. No. Trojan) peptides containing the third helix of the antennapedia homeodomain fused to a peptide mimicking the juxtamembrane (JMP) region of the cytoplasmic domain of N-cadherin (CDH2; 114020) result in the inhibition of both CDH2 and beta-1 integrin (ITGB1; 135630) function. Microscopic analysis showed that expression of JMP, which binds to the cytoplasmic domain of CDH2, results in a reduction of neurite outgrowth on cadherin substrates. Treatment of cells with JMP resulted in the release of FER from the cadherin complex and its accumulation in the integrin complex. The accumulation of FER in the integrin complex and the inhibitory effects of JMP could be reversed with a peptide that mimics the first coiled-coil domain of FER. The results suggested that FER mediates crosstalk between CDH2 and ITGB1. By Southern analysis of somatic cell hybrid DNAs, Krolewski et al. (1990) assigned the TYK3 gene to human chromosome 5. By in situ hybridization, Morris et al. (1990) concluded that the FER gene is located at 5q21-q22. Asada and Nadeau (1994) mapped the mouse homolog, Fert, to chromosome 11 by interspecific backcross analysis.

[13930] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [13931] Arregui, C.; Pathre, P.; Lilien, J.; Balsamo, J. : The nonreceptor tyrosine kinase Fer mediates cross-talk between N-cadherin and beta-1-integrins. *J. Cell Biol.* 149: 1263-1273, 2000. ; and
- [13932] Morris, C.; Heisterkamp, N.; Hao, Q. L.; Testa, J. R.; Groffen, J. : The human tyrosine kinase gene (FER) maps to chromosome 5 and is deleted in myeloid leukemias with a del(5q). *Cytoge.*
- [13933] Further studies establishing the function and utilities of FER are found in John Hopkins OMIM database record ID 176942, and in cited publications numbered 3341, 12361-12362, 507 and 12666 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Baculoviral IAP Repeat-containing 3 (BIRC3, Accession XM_040715) is another VGAM224 host target gene. BIRC3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BIRC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC3 BINDING SITE, designated SEQ ID:33367, to the nucleotide sequence of VGAM224 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2935.

[13934] Another function of VGAM224 is therefore inhibition of Baculoviral IAP Repeat-containing 3 (BIRC3, Accession XM_040715). Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC3. LOC196382 (Accession XM_116913) is another VGAM224 host target gene. LOC196382 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196382 BINDING SITE, designated SEQ ID:43148, to the nucleotide sequence of VGAM224 RNA, herein designated VGAM RNA, also designated SEQ ID:2935.

[13935] Another function of VGAM224 is therefore inhibition of LOC196382 (Accession XM_116913). Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196382. LOC93097 (Accession XM_049221) is another VGAM224 host target gene. LOC93097 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC93097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93097 BINDING SITE, designated SEQ ID:35354, to the nucleotide sequence of VGAM224 RNA, herein designated VGAM RNA, also designated SEQ ID:2935.

[13936] Another function of VGAM224 is therefore inhibition of LOC93097 (Accession XM_049221). Accordingly, utilities of VGAM224 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93097. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 225 (VGAM225) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13937] VGAM225 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM225 was detected is described hereinabove with reference to Figs. 1–8.

[13938] VGAM225 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Callitrichine Herpesvirus 3. VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13939] VGAM225 gene encodes a VGAM225 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM225 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM225 precursor RNA is designated SEQ ID:211, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:211 is located at position 113297 relative to the genome of Callitrichine Herpesvirus 3.

[13940] VGAM225 precursor RNA folds onto itself, forming VGAM225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13941] An enzyme complex designated DICER COMPLEX, `dices` the VGAM225 folded precursor RNA into VGAM225 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM225 RNA is designated SEQ ID:2936, and is provided hereinbelow with reference to the sequence listing part.

[13942] VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM225 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13943] VGAM225 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM225 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM225 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[13944] The complementary binding of VGAM225 RNA, herein designated VGAM RNA, to host target binding sites on VGAM225 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM225 host tar-

get RNA into VGAM225 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13945] It is appreciated that VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM225 host target genes. The mRNA of each one of this plurality of VGAM225 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM225 RNA, herein designated VGAM RNA, and which when bound by VGAM225 RNA causes inhibition of translation of respective one or more VGAM225 host target proteins.

[13946] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM225 gene, herein designated VGAM GENE, on one or more VGAM225 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13947] It is yet further appreciated that a function of VGAM225 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM225 include diagnosis, prevention and treatment of viral infection by Callicitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM225 correlate with, and may be deduced from, the identity of the host target genes which VGAM225 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13948] Nucleotide sequences of the VGAM225 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM225 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM225 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM225 are further

described hereinbelow with reference to Table 1.

[13949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM225 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM225 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13950] As mentioned hereinabove with reference to Fig. 1, a function of VGAM225 gene, herein designated VGAM is inhibition of expression of VGAM225 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM225 correlate with, and may be deduced from, the identity of the target genes which VGAM225 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13951] Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM_002084) is a VGAM225 host target gene. GPX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPX3

BINDING SITE, designated SEQ ID:7878, to the nucleotide sequence of VGAM225 RNA, herein designated VGAM RNA, also designated SEQ ID:2936.

[13952] A function of VGAM225 is therefore inhibition of Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM_002084), a gene which reduces lipid hydroperoxide and H₂O₂ in plasma. Accordingly, utilities of VGAM225 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPX3. The function of GPX3 has been established by previous studies. Glutathione peroxidase (EC 1.11.1.9) catalyzes the reduction of hydrogen peroxide, organic hydroperoxide, and lipid peroxides by reduced glutathione and functions in the protection of cells against oxidative damage. This enzyme, found mainly in the cytosol of mammalian cells, is unusual in its content of a selenocysteine residue in its active site that is encoded by a TGA opal codon (Chambers et al., 1986). The glutathione peroxidase found in plasma is immunologically distinct from the erythrocyte and liver cytosolic enzymes (OMIM Ref. No. 138320). It also has some differences in physical and kinetic properties. Takahashi et al. (1990) isolated cDNA clones coding for plasma GPX. They found that the nu-

cleotide sequence consisted of a 678-bp open reading frame coding for a 226-amino acid polypeptide with a molecular mass of 25,389. The amino acid sequence showed only 44% homology with human cellular GPX. Northern blot analysis showed a single transcript of 2.2 kb in the polyadenylated RNA fractions of human placenta and of a human hepatic cell line, HepG2, but not in those of human liver and endothelial cells. Takahashi et al. (1990) concluded that as the plasma enzyme contains 1 atom of selenium per subunit, the in-frame TGA observed at positions 217–219 could be assigned to selenocysteine. Chu et al. (1992) found that glutathione peroxidase–3 is expressed in kidney, lung, heart, breast, placenta, and, in the human but not the rodent, in liver as well. By Southern analysis of genomic DNA from human/hamster somatic cell hybrids, Chu (1994) mapped the GPX3 gene to chromosome 5.

[13953] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[13954] Chu, F.–F.; Esworthy, R. S.; Doroshov, J. H.; Doan, K.; Liu, X.–F. : Expression of glutathione peroxidase in human liver in addition to kidney, heart, lung, and breast in hu–

mans and rodents. Blood 79: 3233–3238, 1992. ; and

[13955] Takahashi, K.; Akasaka, M.; Yamamoto, Y.; Kobayashi, C.; Mizoguchi, J.; Koyama, J. : Primary structure of human plasma glutathione peroxidase deduced from cDNA sequences. J. Biochem. 108.

[13956] Further studies establishing the function and utilities of GPX3 are found in John Hopkins OMIM database record ID 138321, and in cited publications numbered 374 and 3745–3746 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 226 (VGAM226) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13957] VGAM226 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM226 was detected is described hereinabove with reference to Figs. 1–8.

[13958] VGAM226 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM226 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[13959] VGAM226 gene encodes a VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM226 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM226 precursor RNA is designated SEQ ID:212, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:212 is located at position 82259 relative to the genome of Calitrichine Herpesvirus 3.

[13960] VGAM226 precursor RNA folds onto itself, forming VGAM226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13961] An enzyme complex designated DICER COMPLEX, `dices` the VGAM226 folded precursor RNA into VGAM226 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM226 RNA is designated SEQ ID:2937, and is provided hereinbelow with reference to the sequence listing part.

[13962] VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM226 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13963] VGAM226 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM226 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM226 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13964] The complementary binding of VGAM226 RNA, herein designated VGAM RNA, to host target binding sites on VGAM226 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM226 host target RNA into VGAM226 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[13965] It is appreciated that VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM226 host target genes. The mRNA of each one of this plurality of VGAM226 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM226 RNA, herein designated VGAM RNA, and which when bound by VGAM226 RNA causes inhibition of translation of respective one or more VGAM226 host target proteins.

[13966] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM226 gene, herein designated VGAM GENE, on one or more VGAM226 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13967] It is yet further appreciated that a function of VGAM226 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM226 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM226 correlate with, and may be deduced from, the identity of the host target genes which VGAM226 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13968] Nucleotide sequences of the VGAM226 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM226 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM226 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM226 are further described hereinbelow with reference to Table 1.

[13969] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM226 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM226 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13970] As mentioned hereinabove with reference to Fig. 1, a function of VGAM226 gene, herein designated VGAM is inhibition of expression of VGAM226 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM226 correlate with, and may be deduced from, the identity of the target genes which VGAM226 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13971] MGC1136 (Accession NM_024025) is a VGAM226 host target gene. MGC1136 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC1136, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC1136 BINDING SITE, designated SEQ ID:23453, to the nucleotide sequence of VGAM226 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2937.

[13972] A function of VGAM226 is therefore inhibition of MGC1136 (Accession NM_024025). Accordingly, utilities of VGAM226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC1136. MGC4796 (Accession XM_029031) is another VGAM226 host target gene. MGC4796 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4796, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4796 BINDING SITE, designated SEQ ID:30826, to the nucleotide sequence of VGAM226 RNA, herein designated VGAM RNA, also designated SEQ ID:2937.

[13973] Another function of VGAM226 is therefore inhibition of MGC4796 (Accession XM_029031). Accordingly, utilities of VGAM226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4796. LOC92539 (Accession XM_045632) is another VGAM226 host target gene. LOC92539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92539, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92539 BINDING SITE, designated SEQ ID:34497, to the nucleotide sequence of VGAM226 RNA, herein designated VGAM RNA, also designated SEQ ID:2937.

[13974] Another function of VGAM226 is therefore inhibition of LOC92539 (Accession XM_045632). Accordingly, utilities of VGAM226 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92539. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 227 (VGAM227) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13975] VGAM227 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM227 was detected is described hereinabove with reference to Figs. 1–8.

[13976] VGAM227 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus

3. VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[13977] VGAM227 gene encodes a VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM227 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM227 precursor RNA is designated SEQ ID:213, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:213 is located at position 28474 relative to the genome of Calitrichine Herpesvirus 3.

[13978] VGAM227 precursor RNA folds onto itself, forming VGAM227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[13979] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM227 folded precursor RNA into VGAM227 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM227 RNA is designated SEQ ID:2938, and is provided hereinbelow with reference to the sequence listing part.

[13980] VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM227 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[13981] VGAM227 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM227 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM227 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[13982] The complementary binding of VGAM227 RNA, herein designated VGAM RNA, to host target binding sites on VGAM227 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM227 host target RNA into VGAM227 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[13983] It is appreciated that VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM227 host target genes. The mRNA of each one of this plurality of VGAM227 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM227 RNA, herein designated VGAM RNA, and which when bound by VGAM227 RNA causes inhibition of translation of respective one or more VGAM227 host target proteins.

[13984] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM227 gene, herein designated VGAM GENE, on one or more VGAM227 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[13985] It is yet further appreciated that a function of VGAM227 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM227 correlate with, and may be deduced from, the identity of the host target genes which VGAM227 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[13986] Nucleotide sequences of the VGAM227 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM227 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM227 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM227 are further described hereinbelow with reference to Table 1.

[13987] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM227 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM227 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[13988] As mentioned hereinabove with reference to Fig. 1, a function of VGAM227 gene, herein designated VGAM is inhibition of expression of VGAM227 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM227 correlate with, and may be deduced from, the identity of the target genes which VGAM227 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[13989] TRIM (Accession NM_016388) is a VGAM227 host target gene. TRIM BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM BINDING SITE, designated SEQ ID:18532, to the nucleotide sequence of VGAM227 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2938.

[13990] A function of VGAM227 is therefore inhibition of TRIM (Accession NM_016388), a gene which plays a role in recruiting signaling proteins to the plasma membrane upon T-cell receptor (TCR) complex activation in T cells. Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM. The function of TRIM has been established by previous studies. T-cell activation requires stimulation of the T-cell receptor (TCR; OMIM Ref. No. 186880)–CD3 (see OMIM Ref. No. CD3Z; 186780) complex, followed by recruitment of an array of intracellular signaling proteins (e.g., GRB2 (OMIM Ref. No. 108355) and PLCG1 (OMIM Ref. No. 172420)). Mediating the interaction between the extracellular receptors and intracellular signaling pathways are adaptor proteins such as LAT (OMIM Ref. No. 602354). Bruyns et al. (1998) purified a 29/30-kD disulfide-linked dimeric phosphoprotein, which they called TRIM (TCR-interacting molecule), that associates and comodulates with the TCR–CD3 complex in T lymphocytes. By tryptic peptide sequence analysis and touchdown PCR analysis of a T-cell cDNA library, they isolated a cDNA encoding TRIM. Sequence analysis predicted

that TRIM is a 186-amino acid type III transmembrane protein containing an 8-amino acid extracellular domain, which includes a cys residue, and a 19-amino acid transmembrane region that lacks charged residues. The intracellular portion possesses 4 potential phosphorylation sites and 8 tyrosine residues, at least 3 of which may be involved in Src (OMIM Ref. No. 190090) homology 2 (SH2)-mediated interactions with other signaling proteins. Northern blot analysis detected preferential expression of an approximately 2.0-kb TRIM transcript in thymus, with weaker expression in spleen, lymph nodes, and peripheral blood leukocytes. Western blot analysis of hematopoietic cell lines detected TRIM protein in T cell lines and, to a lesser extent, in natural killer cell lines, but not in B cell lines or in a monocytic cell line. Immunofluorescence and Western blot analyses showed that TRIM is localized in the cell membrane and is associated with CD3E (OMIM Ref. No. 186830) and CD3Z. The authors found that after T-cell activation, TRIM is phosphorylated by Src kinases on tyrosine residues, then associates with PIK3R1 (OMIM Ref. No. 171833).

[13991] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [13992] Bruyns, E.; Marie-Cardine, A.; Kirchgessner, H.; Sagolla, K.; Shevchenko, A.; Mann, M.; Autschbach, F.; Bensussan, A.; Meuer, S.; Schraven, B. : T cell receptor (TCR) interacting molecule (TRIM), a novel disulfide-linked dimer associated with the TCR-CD3-zeta complex, recruits intracellular signaling proteins to the plasma membrane. J. Exp. Med. 188: 561-575, 1998. ; and
- [13993] Hubener, C.; Mincheva, A.; Lichter, P.; Schraven, B.; Bruyns, E. : Genomic organization and chromosomal localization of the human gene encoding the T-cell receptor-interacting molecule.
- [13994] Further studies establishing the function and utilities of TRIM are found in John Hopkins OMIM database record ID 604962, and in cited publications numbered 5002 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ22060 (Accession NM_024612) is another VGAM227 host target gene. FLJ22060 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of FLJ22060 BINDING SITE, designated SEQ ID:23867, to the nucleotide sequence of VGAM227 RNA, herein designated VGAM RNA, also designated SEQ ID:2938.

[13995] Another function of VGAM227 is therefore inhibition of FLJ22060 (Accession NM_024612). Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22060. HBP1 (Accession NM_012257) is another VGAM227 host target gene. HBP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HBP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HBP1 BINDING SITE, designated SEQ ID:14563, to the nucleotide sequence of VGAM227 RNA, herein designated VGAM RNA, also designated SEQ ID:2938.

[13996] Another function of VGAM227 is therefore inhibition of HBP1 (Accession NM_012257). Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HBP1. LOC148823 (Accession NM_145278) is another VGAM227

host target gene. LOC148823 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148823, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148823 BINDING SITE, designated SEQ ID:29795, to the nucleotide sequence of VGAM227 RNA, herein designated VGAM RNA, also designated SEQ ID:2938.

[13997] Another function of VGAM227 is therefore inhibition of LOC148823 (Accession NM_145278). Accordingly, utilities of VGAM227 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148823. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 228 (VGAM228) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[13998] VGAM228 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM228 was detected is described

hereinabove with reference to Figs. 1–8.

[13999] VGAM228 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Calitrichine Herpesvirus 3. VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14000] VGAM228 gene encodes a VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM228 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM228 precursor RNA is designated SEQ ID:214, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:214 is located at position 130971 relative to the genome of Calitrichine Herpesvirus 3.

[14001] VGAM228 precursor RNA folds onto itself, forming VGAM228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14002] An enzyme complex designated DICER COMPLEX, `dices` the VGAM228 folded precursor RNA into VGAM228 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM228 RNA is designated SEQ ID:2939, and is provided hereinbelow with reference to the sequence listing part.

[14003] VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM228 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14004] VGAM228 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM228 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM228 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM228 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14005] The complementary binding of VGAM228 RNA, herein designated VGAM RNA, to host target binding sites on VGAM228 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM228 host target RNA into VGAM228 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14006] It is appreciated that VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM228 host target genes. The mRNA of each one of this plurality of VGAM228 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM228 RNA, herein designated VGAM RNA, and which when bound by VGAM228 RNA causes inhibition of translation of respective one or more VGAM228 host target proteins.

[14007] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM228 gene, herein designated VGAM GENE, on one or more VGAM228 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14008] It is yet further appreciated that a function of VGAM228 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM228 correlate with, and may be deduced from, the identity of the host target genes which VGAM228 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14009] Nucleotide sequences of the VGAM228 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM228 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM228 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM228 are further described hereinbelow with reference to Table 1.

[14010] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM228 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM228 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14011] As mentioned hereinabove with reference to Fig. 1, a function of VGAM228 gene, herein designated VGAM is inhibition of expression of VGAM228 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM228 correlate with, and may be deduced from, the identity of the target genes which VGAM228 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14012] Forkhead Box O1A (rhabdomyosarcoma) (FOXO1A, Accession NM_002015) is a VGAM228 host target gene. FOXO1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXO1A, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXO1A BINDING SITE, designated SEQ ID:7760, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14013] A function of VGAM228 is therefore inhibition of Forkhead Box O1A (rhabdomyosarcoma) (FOXO1A, Accession NM_002015), a gene which is a probable transcription factor. Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXO1A. The function of FOXO1A has been established by previous studies. In alveolar rhabdomyosarcoma, the translocation t(2;13)(q35;q14) is frequently found. Barr et al. (1993) determined that PAX3 (OMIM Ref. No. 606597), which had previously been found to be mutated in Waardenburg syndrome (OMIM Ref. No. 193500), was affected by this t(2;13) in alveolar rhabdomyosarcoma (OMIM Ref. No. 268220). Galili et al. (1993) isolated the chromosome 13 gene that is fused with PAX3. The rearrangement breakpoints occurred within an intron downstream of the paired box and homeodomain-encoding regions. and identified it as a member

of the forkhead domain family, which encodes transcription factors containing a conserved DNA-binding motif related to the *Drosophila* region-specific homeotic gene 'forkhead.' The distal half of the forkhead and the C-terminal region of the FKHR gene are involved in the chimeric transcript and fusion protein. (Because of the homology to 'forkhead,' the gene was symbolized FKHR, for 'forkhead' in rhabdomyosarcoma.) See human T-cell leukemia virus enhancer factor (OMIM Ref. No. 143089) and interleukin enhancer binding factor (OMIM Ref. No. 147685) for other members of the forkhead domain family of transcription factors. Fredericks et al. (1995) demonstrated expression of a 97-kD PAX3/FKHR fusion protein in a t(2;13)-positive rhabdomyosarcoma cell line and verified that a single polypeptide contained epitopes derived from each protein. The fusion protein was localized to the nucleus in these cells, as was wildtype PAX3 in cells lacking the translocation. They found that DNA binding of the fusion protein was significantly impaired relative to that of PAX3 despite the fact that the 2 proteins had identical PAX DNA-binding domains. However, the fusion protein was a much more potent transcriptional activator than PAX3. Thus, the fusion protein may function as

an oncogenic transcription factor by enhancing activation of normal PAX3 target genes.

[14014] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14015] Barr, F. G.; Galili, N.; Holick, J.; Biegel, J. A.; Rovera, G.; Emanuel, B. S. : Rearrangement of the PAX3 paired box gene in the paediatric solid tumor alveolar rhabdomyosarcoma. Nature Genet. 3: 113–117, 1993. ; and

[14016] Fredericks, W. J.; Galili, N.; Mukhopadhyay, S.; Rovera, G.; Bennicelli, J.; Barr, F. G.; Rauscher, F. J., III : The PAX3–FKHR fusion protein created by the t(2;13) translocation in alve.

[14017] Further studies establishing the function and utilities of FOXO1A are found in John Hopkins OMIM database record ID 136533, and in cited publications numbered 12164–12170, 1219 and 2126–2128 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. HUS1 Checkpoint Homolog (*S. pombe*) (HUS1, Accession XM_165873) is another VGAM228 host target gene. HUS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HUS1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HUS1 BINDING SITE, designated SEQ ID:43789, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14018] Another function of VGAM228 is therefore inhibition of HUS1 Checkpoint Homolog (*S. pombe*) (HUS1, Accession XM_165873), a gene which May form DNA damage-responsive protein complex . Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HUS1. The function of HUS1 has been established by previous studies. The *S. pombe* 'checkpoint rad' genes *hus1*, *rad1* (OMIM Ref. No. 603153), *rad3*, *rad9* (OMIM Ref. No. 603761), *rad17* (OMIM Ref. No. 603139), and *rad26* are essential for both the incomplete DNA replication (S-M) and DNA damage checkpoints. An early step in the DNA damage checkpoint response appears to involve activation of the *rad3* phosphatidylinositol 3-kinase-related (PIK-R) checkpoint kinase (see OMIM Ref. No. AT; 208900) by the other 5 checkpoint rad gene products. Kostrub et al. (1998) found that the fission yeast *hus1* and *rad1* proteins

form a stable complex, and that the formation of this complex is dependent on rad9, suggesting that these 3 proteins may exist in a discrete complex in the absence of checkpoint activation. Hus1 is phosphorylated in response to DNA damage, and this phosphorylation requires rad3 and the other checkpoint rad genes. By searching EST databases, Kostrub et al. (1998) and Dean et al. (1998) each identified mouse and human cDNAs encoding hus1 homologs. Kostrub et al. (1998) reported that the predicted 281-amino acid human protein shares 30% and 86% identity with *S. pombe* hus1 and mouse Hus1, respectively. However, neither mammalian gene complemented a fission yeast hus1 mutation. Volkmer and Karnitz (1999) demonstrated that the human RAD1 and HUS1 proteins associate in a complex that interacts with a highly modified form of RAD9. They concluded that these 3 proteins are central components of a DNA damage-responsive protein complex in human cells. AU-rich elements (AREs) are cis-acting sequences typically found in 3-prime untranslated regions of many labile mRNAs. AREs either mediate rapid degradation of mRNA or inhibit its translation. Dominguez et al. (1998) identified EE2-16C, a HUS1 cDNA, among a collection of ARE-containing mR-

NAs.

- [14019] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [14020] Kostrub, C. F.; Knudsen, K.; Subramani, S.; Enoch, T. : Hus1p, a conserved fission yeast checkpoint protein, interacts with Rad1p and is phosphorylated in response to DNA damage. EMBO J. 17: 2055–2066, 1998. ; and
- [14021] Volkmer, E.; Karnitz, L. M. : Human homologs of Schizosaccharomyces pombe Rad1, Hus1, and Rad9 form a DNA damage–responsive protein complex. J. Biol. Chem. 274: 567–570, 1999.
- [14022] Further studies establishing the function and utilities of HUS1 are found in John Hopkins OMIM database record ID 603760, and in cited publications numbered 690, 7624–762 and 2422 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Basic, Immunoglobulin–like Variable Motif Containing (BIVM, Accession NM_017693) is another VGAM228 host target gene. BIVM BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BIVM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BIND–

ING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIVM BINDING SITE, designated SEQ ID:19253, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14023] Another function of VGAM228 is therefore inhibition of Basic, Immunoglobulin-like Variable Motif Containing (BIVM, Accession NM_017693). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIVM. Chromosome 6 Open Reading Frame 37 (C6orf37, Accession XM_041375) is another VGAM228 host target gene. C6orf37 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C6orf37, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C6orf37 BINDING SITE, designated SEQ ID:33516, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14024] Another function of VGAM228 is therefore inhibition of Chromosome 6 Open Reading Frame 37 (C6orf37, Acces-

sion XM_041375). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C6orf37. KIAA1615 (Accession XM_044021) is another VGAM228 host target gene. KIAA1615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1615, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1615 BINDING SITE, designated SEQ ID:34089, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14025] Another function of VGAM228 is therefore inhibition of KIAA1615 (Accession XM_044021). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1615. p21(CDKN1A)-activated Kinase 7 (PAK7, Accession XM_045653) is another VGAM228 host target gene. PAK7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PAK7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PAK7 BINDING SITE, designated SEQ ID:34508, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14026] Another function of VGAM228 is therefore inhibition of p21(CDKN1A)-activated Kinase 7 (PAK7, Accession XM_045653). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAK7. SMOC2 (Accession XM_051452) is another VGAM228 host target gene. SMOC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SMOC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SMOC2 BINDING SITE, designated SEQ ID:35833, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14027] Another function of VGAM228 is therefore inhibition of SMOC2 (Accession XM_051452). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SMOC2.

LOC150372 (Accession XM_086893) is another VGAM228 host target gene. LOC150372 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150372, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150372 BINDING SITE, designated SEQ ID:38937, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14028] Another function of VGAM228 is therefore inhibition of LOC150372 (Accession XM_086893). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150372. LOC151760 (Accession XM_098117) is another VGAM228 host target gene. LOC151760 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151760 BINDING SITE, designated SEQ ID:41388, to the nucleotide sequence of VGAM228 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2939.

[14029] Another function of VGAM228 is therefore inhibition of LOC151760 (Accession XM_098117). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151760. LOC221300 (Accession XM_166322) is another VGAM228 host target gene. LOC221300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221300, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221300 BINDING SITE, designated SEQ ID:44146, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14030] Another function of VGAM228 is therefore inhibition of LOC221300 (Accession XM_166322). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221300. LOC221489 (Accession XM_168066) is another VGAM228 host target gene. LOC221489 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221489, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221489 BINDING SITE, designated SEQ ID:44982, to the nucleotide sequence of VGAM228 RNA, herein designated VGAM RNA, also designated SEQ ID:2939.

[14031] Another function of VGAM228 is therefore inhibition of LOC221489 (Accession XM_168066). Accordingly, utilities of VGAM228 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221489. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 229 (VGAM229) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14032] VGAM229 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM229 was detected is described hereinabove with reference to Figs. 1–8.

[14033] VGAM229 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus

3. VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14034] VGAM229 gene encodes a VGAM229 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM229 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM229 precursor RNA is designated SEQ ID:215, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:215 is located at position 61747 relative to the genome of Calitrichine Herpesvirus 3.

[14035] VGAM229 precursor RNA folds onto itself, forming VGAM229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14036] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM229 folded precursor RNA into VGAM229 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM229 RNA is designated SEQ ID:2940, and is provided hereinbelow with reference to the sequence listing part.

[14037] VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM229 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14038] VGAM229 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM229 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM229 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14039] The complementary binding of VGAM229 RNA, herein designated VGAM RNA, to host target binding sites on VGAM229 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM229 host target RNA into VGAM229 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14040] It is appreciated that VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM229 host target genes. The mRNA of each one of this plurality of VGAM229 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM229 RNA, herein designated VGAM RNA, and which when bound by VGAM229 RNA causes inhibition of translation of respective one or more VGAM229 host target proteins.

[14041] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM229 gene, herein designated VGAM GENE, on one or more VGAM229 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14042] It is yet further appreciated that a function of VGAM229 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM229 correlate with, and may be deduced from, the identity of the host target genes which VGAM229 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14043] Nucleotide sequences of the VGAM229 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM229 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM229 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM229 are further described hereinbelow with reference to Table 1.

[14044] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM229 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM229 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14045] As mentioned hereinabove with reference to Fig. 1, a function of VGAM229 gene, herein designated VGAM is inhibition of expression of VGAM229 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM229 correlate with, and may be deduced from, the identity of the target genes which VGAM229 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14046] ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164) is a VGAM229 host target gene. ABCD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ABCD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCD2 BINDING SITE, designated SEQ

ID:11657, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14047] A function of VGAM229 is therefore inhibition of ATP-binding Cassette, Sub-family D (ALD), Member 2 (ABCD2, Accession NM_005164), a gene which probable transporter. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCD2. The function of ABCD2 has been established by previous studies. Lombard-Platet et al. (1996) described the cloning and characterization of a mouse Ald-related gene, symbolized Aldr by them, that codes for a 741-amino acid protein sharing the same half-ABC transporter structure and 66% amino acid identity with the protein that is mutant in X-linked adrenoleukodystrophy (ALD; 300100). PMP70 (OMIM Ref. No. 170995), another half-ABC transporter in the peroxisomal membrane protein, had 38% sequence identity to the mouse Aldr protein. Lombard-Platet et al. (1996) showed that the mouse Aldr protein is associated with peroxisomes. The mouse Ald and Aldr genes show overlapping but distinctive expression patterns. Interestingly, at least in mouse, Aldr is expressed at high levels in brain

and adrenal, 2 organs with major involvement in adrenoleukodystrophy. Using oligonucleotide primers designed from the mouse sequence, the authors PCR-amplified 2 overlapping fragments of an 866-bp segment from human genomic DNA. This segment from the human ALDR ortholog shares 90% amino acid identity with the mouse protein. Lombard-Platet et al. (1996) speculated that the human gene may be a candidate for a modifier gene that accounts for some of the extreme phenotypic variability of ALD. The human ALDR gene was also a candidate for 1 of the complementation groups of Zellweger syndrome (see OMIM Ref. No. 214100), a genetically heterogeneous disorder of peroxisomal biogenesis. By isotopic in situ hybridization, Savary et al. (1997) mapped the ALDR gene to 12q11-q12 and its murine homolog to a region of homology of synteny on mouse chromosome 15. The mapping to chromosome 12 was confirmed by PCR analysis of a panel of whole genome radiation hybrids.

[14048] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14049] Lombard-Platet, G.; Savary, S.; Sarde, C.-O.; Mandel, J.-L.;

Chimini, G. : A close relative of the adrenoleukodystrophy (ALD) gene codes for a peroxisomal protein with a specific expression pattern. Proc. Nat. Acad. Sci. 93: 1265–1269, 1996. ; and

[14050] Savary, S.; Troffer–Charlier, N.; Gyapay, G.; Mattei, M.–G.; Chimini, G. : Chromosomal localization of the adrenoleukodystrophy–related gene in man and mice. Europ. J. Hum. Genet. 5: 99–.

[14051] Further studies establishing the function and utilities of ABCD2 are found in John Hopkins OMIM database record ID 601081, and in cited publications numbered 1259–126 and 8796 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v–erb–b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228) is another VGAM229 host target gene. EGFR BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EGFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFR BINDING SITE, designated SEQ ID:11721, to the nucleotide sequence of VGAM229 RNA,

herein designated VGAM RNA, also designated SEQ ID:2940.

[14052] Another function of VGAM229 is therefore inhibition of Epidermal Growth Factor Receptor (erythroblastic leukemia viral (v-erb-b) Oncogene Homolog, Avian) (EGFR, Accession NM_005228), a gene which is a receptor for egf, but also for other members of the egf family. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFR. The function of EGFR has been established by previous studies. Maternal uniparental disomy (UPD) of chromosome 7 has been reported in approximately 10% of cases of Silver-Russell syndrome (SRS; 180860). This suggests that at least 1 gene on chromosome 7 is imprinted and involved in the pathogenesis of SRS. Wakeling et al. (1998) investigated the EGFR gene as a candidate for imprinting because the gene maps to 7p12, a region homologous to an imprinted region on mouse chromosome 11. Using a restriction fragment length polymorphism, they found, however, biallelic expression of EGFR in a range of normal human fetal tissues. Expression was also demonstrated in fibroblasts and lymphoblasts from SRS patients with maternal UPD7. Thus, no

evidence that EGFR is imprinted was found, making its involvement in SRS unlikely. However, EGFR was shown to be widely expressed in the human fetus, providing evidence that it plays an important role in early development. The only gene known to be imprinted on chromosome 7 at that time was MEST, also called paternally expressed gene-1 (OMIM Ref. No. 601029), which maps to 7q32. Animal model experiments lend further support to the function of EGFR. Activation of epidermal growth factor receptor triggers mitogenic signaling in gastrointestinal mucosa, and its expression is also upregulated in colon cancers and most neoplasms. Pai et al. (2002) investigated whether prostaglandins transactivate EGFR. Pai et al. (2002) demonstrated that prostaglandin E2 (PGE2; 176804) rapidly phosphorylates EGFR and triggers the extracellular signal-regulated kinase 2 (ERK2; 176948)-mitogenic signaling pathway in normal gastric epithelial and colon cancer cell lines. Inactivation of EGFR kinase with selective inhibitors significantly reduced PGE2-induced ERK2 activation, c-fos mRNA expression, and cell proliferation. Inhibition of matrix metalloproteinases, TGFA, or c-Src (OMIM Ref. No. 190090) blocked PGE2-mediated EGFR transactivation and downstream sig-

naling, indicating that PGE2-induced EGFR transactivation involves signaling transduced via TGF-alpha, an EGFR ligand, likely released by c-Src-activated MMPs.

[14053] It is appreciated that the abovementioned animal model for EGFR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14054] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14055] Pai, R.; Soreghan, B.; Szabo, I. L.; Pavelka, M.; Baatar, D.; Tarnawski, A. S. : Prostaglandin E2 transactivates EGF receptor: a novel mechanism for promoting colon cancer growth and gastrointestinal hypertrophy. Nature Med. 8: 289-293, 2002. ; and

[14056] Wakeling, E. L.; Abu-Amero, S. N.; Stanier, P.; Preece, M. A.; Moore, G. E. : Human EGFR, a candidate gene for the Silver-Russell syndrome, is biallelically expressed in a wide range.

[14057] Further studies establishing the function and utilities of EGFR are found in John Hopkins OMIM database record ID 131550, and in cited publications numbered 4645-4649, 369-377, 422 and 4587-4597 listed in the bibliography

section hereinbelow, which are also hereby incorporated by refer-

ence.UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7)

(GALNT7, Accession NM_017423) is another VGAM229 host target gene. GALNT7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALNT7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALNT7 BINDING SITE, designated SEQ ID:18878, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14058] Another function of VGAM229 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7) (GALNT7, Accession NM_017423). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALNT7. Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530) is another VGAM229 host target gene. HIF1A BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HIF1A BINDING SITE, designated SEQ ID:7266, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14059] Another function of VGAM229 is therefore inhibition of Hypoxia-inducible Factor 1, Alpha Subunit (basic helix-loop-helix transcription factor) (HIF1A, Accession NM_001530), a gene which is a basic helix-loop-helix transcription factor and mediates transcriptional responses to hypoxia and dioxin-signaling. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HIF1A. The function of HIF1A has been established by previous studies. HIF1 has a key role in cellular response to hypoxia, including the regulation of genes involved in energy metabolism, angiogenesis, and apoptosis. The alpha subunits of HIF are rapidly degraded by the proteasome under normal conditions but are stabilized by hypoxia. Cobaltous ions or iron chelators mimic hypoxia, in-

dicating that the stimuli may interact through effects on a ferroprotein oxygen sensor. Maxwell et al. (1999) demonstrated a critical role for the von Hippel–Lindau tumor suppressor gene product VHL (OMIM Ref. No. 193300) in HIF1 regulation. In VHL-defective cells, HIF- α subunits were constitutively stabilized and HIF1 was activated. Reexpression of VHL restored oxygen-dependent instability. VHL and HIF- α subunits coimmunoprecipitated, and VHL was present in the hypoxic HIF1 DNA-binding complex. In cells exposed to iron chelation or cobaltous ions, HIF1 is dissociated from VHL. These findings indicated that the interaction between HIF1 and VHL is iron dependent and that it is necessary for the oxygen-dependent degradation of HIF- α subunits. Maxwell et al. (1999) suggested that constitutive HIF1 activation may underlie the angiogenic phenotype of VHL-associated tumors. Animal model experiments lend further support to the function of HIF1A. To investigate whether HIF1 is required for ventilatory responses to hypoxia, Kline et al. (2002) analyzed mice that were either wildtype or heterozygous for a loss-of-function (knockout) allele at the Hif1a locus. Although ventilatory response to acute hypoxia was not impaired in heterozygous Hif1a mice, the

response was primarily mediated via vagal afferents, whereas in wildtype mice, carotid body chemoreceptors played a predominant role. When carotid bodies isolated from wildtype mice were exposed to either cyanide or hypoxia, a marked increase in sinus nerve activity was recorded. In contrast, carotid bodies from heterozygous mice responded to cyanide but not to hypoxia. Histologic analysis revealed no abnormalities of carotid body morphology in heterozygous mice. Wildtype mice exposed to hypoxia for 3 days manifested an augmented ventilatory response to a subsequent acute hypoxic challenge. In contrast, prior chronic hypoxia resulted in a diminished ventilatory response to acute hypoxia in heterozygous Hif1a mice. Thus, partial HIF1A deficiency has a dramatic effect on carotid body neural activity and ventilatory adaptation to chronic hypoxia.

[14060] It is appreciated that the abovementioned animal model for HIF1A is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14061] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [14062] Maxwell, P. H.; Wiesener, M. S.; Chang, G.-W.; Clifford, S. C.; Vaux, E. C.; Cockman, M. E.; Wykoff, C. C.; Pugh, C. W.; Maher, E. R.; Ratcliffe, P. J. : The tumour suppressor protein VHL targets hypoxia-inducible factors for oxygen-dependent proteolysis. *Nature* 399: 271-275, 1999. ; and
- [14063] Kline, D. D.; Peng, Y.-J.; Manalo, D. J.; Semenza, G. L.; Prabhakar, N. R. : Defective carotid body function and impaired ventilatory responses to chronic hypoxia in mice partially defi.
- [14064] Further studies establishing the function and utilities of HIF1A are found in John Hopkins OMIM database record ID 603348, and in cited publications numbered 5343, 4366, 2691, 7997, 7998-8005, 436 and 8006-8008 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804) is another VGAM229 host target gene. MEN1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MEN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEN1 BINDING SITE, designated SEQ ID:44844, to the nucleotide sequence of

VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14065] Another function of VGAM229 is therefore inhibition of Multiple Endocrine Neoplasia I (MEN1, Accession XM_167804). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEN1. Myosin IB (MYO1B, Accession NM_012223) is another VGAM229 host target gene. MYO1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MYO1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1B BINDING SITE, designated SEQ ID:14523, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14066] Another function of VGAM229 is therefore inhibition of Myosin IB (MYO1B, Accession NM_012223). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO1B. Transducin (beta)-like 2 (TBL2, Accession NM_012453) is another VGAM229 host target gene. TBL2

BINDING SITE1 and TBL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TBL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBL2 BINDING SITE1 and TBL2 BINDING SITE2, designated SEQ ID:14821 and SEQ ID:26867 respectively, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14067] Another function of VGAM229 is therefore inhibition of Transducin (beta)-like 2 (TBL2, Accession NM_012453), a gene which is of unknown function. Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TBL2. The function of TBL2 has been established by previous studies. Meng et al. (1998) constructed a physical map encompassing the 1.5-Mb region of chromosome 7q11.23 that is commonly deleted in Williams-Beuren syndrome (WBS; 194050). They identified 3 genes within this region, including TBL2, which they designated WS-beta-TRP. By EST database searching, screening of a testis cDNA library, and sequencing, they cloned a TBL2 cDNA

encoding a deduced 426–amino acid protein with 4 WD (or beta–transducin) repeats. TBL2 shares approximately 40% homology with a hypothetical *C. elegans* protein, suggesting that the gene has been conserved through evolution. Northern blot analysis detected a 2.4–kb transcript in all tissues examined, with high expression in heart, brain, placenta, skeletal muscle, and pancreas. Perez Jurado et al. (1999) cloned a TBL2 cDNA from a fetal brain cDNA library and found that it encodes a deduced 447–amino acid protein with a predicted molecular mass of 49.8 kD. They also cloned the mouse ortholog, which shares 84% sequence identity with the human protein. Northern blot analysis of human tissues detected not only the 2.4–kb transcript, but an approximately 5–kb transcript which was ubiquitously expressed at lower levels. Perez Jurado et al. (1999) also identified an alternatively spliced transcript containing an additional exon (exon 2–prime) with an inframe stop codon that encodes a deduced 75–amino acid protein with 43 amino acids identical to TBL2 at the N terminus and no known functional domain.

[14068] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[14069] Meng, X.; Lu, X.; Li, Z.; Green, E. D.; Massa, H.; Trask, B. J.; Morris, C. A.; Keating, M. T. : Complete physical map of the common deletion region in Williams syndrome and identification and characterization of three novel genes. Hum. Genet. 103: 590–599, 1998. ; and

[14070] Perez Jurado, L. A.; Wang, Y.–K.; Francke, U.; Cruces, J. : TBL2, a novel transducin family member in the WBS deletion: characterization of the complete sequence, genomic structure, tra.

[14071] Further studies establishing the function and utilities of TBL2 are found in John Hopkins OMIM database record ID 605842, and in cited publications numbered 97 and 6619 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM_032852) is another VGAM229 host target gene. AUTL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AUTL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AUTL1 BINDING SITE, designated SEQ

ID:26645, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14072] Another function of VGAM229 is therefore inhibition of AUT-like 1, Cysteine Endopeptidase (*S. cerevisiae*) (AUTL1, Accession NM_032852). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AUTL1. B1 (Accession NM_014451) is another VGAM229 host target gene. B1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B1 BINDING SITE, designated SEQ ID:15800, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14073] Another function of VGAM229 is therefore inhibition of B1 (Accession NM_014451). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B1. BCL2-associated Athanogene 5 (BAG5, Accession NM_004873) is another VGAM229 host target gene. BAG5

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BAG5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAG5 BINDING SITE, designated SEQ ID:11305, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14074] Another function of VGAM229 is therefore inhibition of BCL2-associated Athanogene 5 (BAG5, Accession NM_004873). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BAG5. CDK5 Regulatory Subunit Associated Protein 3 (CDK5RAP3, Accession NM_025197) is another VGAM229 host target gene. CDK5RAP3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDK5RAP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDK5RAP3 BINDING SITE, designated SEQ ID:24851, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ

ID:2940.

[14075] Another function of VGAM229 is therefore inhibition of CDK5 Regulatory Subunit Associated Protein 3 (CDK5RAP3, Accession NM_025197). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDK5RAP3. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380) is another VGAM229 host target gene. DDX28 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DDX28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX28 BINDING SITE, designated SEQ ID:20410, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14076] Another function of VGAM229 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 28 (DDX28, Accession NM_018380). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX28. DKFZP434L187 (Accession XM_044070) is another

VGAM229 host target gene. DKFZP434L187 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434L187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434L187 BINDING SITE, designated SEQ ID:34117, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14077] Another function of VGAM229 is therefore inhibition of DKFZP434L187 (Accession XM_044070). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434L187. FLJ13322 (Accession NM_024722) is another VGAM229 host target gene. FLJ13322 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13322 BINDING SITE, designated SEQ ID:24059, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14078] Another function of VGAM229 is therefore inhibition of FLJ13322 (Accession NM_024722). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13322. FLJ14564 (Accession XM_084459) is another VGAM229 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564 BINDING SITE, designated SEQ ID:37593, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14079] Another function of VGAM229 is therefore inhibition of FLJ14564 (Accession XM_084459). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14564. FLJ20086 (Accession NM_017661) is another VGAM229 host target gene. FLJ20086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20086, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20086 BINDING SITE, designated SEQ ID:19188, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14080] Another function of VGAM229 is therefore inhibition of FLJ20086 (Accession NM_017661). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20086. FLJ20445 (Accession NM_017824) is another VGAM229 host target gene. FLJ20445 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20445, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20445 BINDING SITE, designated SEQ ID:19480, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14081] Another function of VGAM229 is therefore inhibition of FLJ20445 (Accession NM_017824). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20445.

G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_139201) is another VGAM229 host target gene. GIT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GIT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GIT2 BINDING SITE, designated SEQ ID:29212, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14082] Another function of VGAM229 is therefore inhibition of G Protein-coupled Receptor Kinase-interactor 2 (GIT2, Accession NM_139201). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GIT2. H2A Histone Family, Member J (H2AFJ, Accession NM_018267) is another VGAM229 host target gene. H2AFJ BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by H2AFJ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H2AFJ BINDING SITE, designated SEQ ID:20236, to the nucleotide se-

quence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14083] Another function of VGAM229 is therefore inhibition of H2A Histone Family, Member J (H2AFJ, Accession NM_018267). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H2AFJ. NPD009 (Accession XM_170795) is another VGAM229 host target gene. NPD009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NPD009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPD009 BINDING SITE, designated SEQ ID:45562, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14084] Another function of VGAM229 is therefore inhibition of NPD009 (Accession XM_170795). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NPD009. Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_144498) is another VGAM229 host target gene. OS-

BPL2 BINDING SITE1 and OSBPL2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OSBPL2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OSBPL2 BINDING SITE1 and OSBPL2 BINDING SITE2, designated SEQ ID:29317 and SEQ ID:16849 respectively, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14085] Another function of VGAM229 is therefore inhibition of Oxysterol Binding Protein-like 2 (OSBPL2, Accession NM_144498). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OSBPL2. Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM_003342) is another VGAM229 host target gene. UBE2G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G1 BINDING SITE,

designated SEQ ID:9348, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14086] Another function of VGAM229 is therefore inhibition of Ubiquitin-conjugating Enzyme E2G 1 (UBC7 homolog, *C. elegans*) (UBE2G1, Accession NM_003342). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G1. LOC133418 (Accession XM_059649) is another VGAM229 host target gene. LOC133418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC133418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133418 BINDING SITE, designated SEQ ID:37037, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14087] Another function of VGAM229 is therefore inhibition of LOC133418 (Accession XM_059649). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133418. LOC143098 (Accession XM_084421) is an-

other VGAM229 host target gene. LOC143098 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC143098, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143098 BINDING SITE, designated SEQ ID:37575, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14088] Another function of VGAM229 is therefore inhibition of LOC143098 (Accession XM_084421). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143098. LOC145622 (Accession XM_085186) is another VGAM229 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37910, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14089] Another function of VGAM229 is therefore inhibition of LOC145622 (Accession XM_085186). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC148195 (Accession XM_097419) is another VGAM229 host target gene. LOC148195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148195 BINDING SITE, designated SEQ ID:40872, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14090] Another function of VGAM229 is therefore inhibition of LOC148195 (Accession XM_097419). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148195. LOC221510 (Accession XM_165807) is another VGAM229 host target gene. LOC221510 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221510, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221510 BINDING SITE, designated SEQ ID:43769, to the nucleotide sequence of VGAM229 RNA, herein designated VGAM RNA, also designated SEQ ID:2940.

[14091] Another function of VGAM229 is therefore inhibition of LOC221510 (Accession XM_165807). Accordingly, utilities of VGAM229 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221510. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 230 (VGAM230) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14092] VGAM230 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM230 was detected is described hereinabove with reference to Figs. 1–8.

[14093] VGAM230 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM230 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[14094] VGAM230 gene encodes a VGAM230 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM230 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM230 precursor RNA is designated SEQ ID:216, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:216 is located at position 57457 relative to the genome of Calitrichine Herpesvirus 3.

[14095] VGAM230 precursor RNA folds onto itself, forming VGAM230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM230 folded precursor RNA into VGAM230 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM230 RNA is designated SEQ ID:2941, and is provided hereinbelow with reference to the sequence listing part.

[14097] VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM230 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14098] VGAM230 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM230 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM230 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14099] The complementary binding of VGAM230 RNA, herein designated VGAM RNA, to host target binding sites on VGAM230 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM230 host target RNA into VGAM230 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[14100] It is appreciated that VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM230 host target genes. The mRNA of each one of this plurality of VGAM230 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM230 RNA, herein designated VGAM RNA, and which when bound by VGAM230 RNA causes inhibition of translation of respective one or more VGAM230 host target proteins.

[14101] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM230 gene, herein designated VGAM GENE, on one or more VGAM230 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14102] It is yet further appreciated that a function of VGAM230 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of viral infection by Callicitricine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM230 correlate with, and may be deduced from, the identity of the host target genes which VGAM230 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14103] Nucleotide sequences of the VGAM230 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM230 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM230 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM230 are further described hereinbelow with reference to Table 1.

[14104] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM230 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM230 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM230 gene, herein designated VGAM is inhibition of expression of VGAM230 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM230 correlate with, and may be deduced from, the identity of the target genes which VGAM230 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14106] Ciliary Neurotrophic Factor Receptor (CNTFR, Accession NM_001842) is a VGAM230 host target gene. CNTFR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTFR BINDING SITE, designated SEQ ID:7577, to the nucleotide sequence of VGAM230 RNA, herein designated

VGAM RNA, also designated SEQ ID:2941.

[14107] A function of VGAM230 is therefore inhibition of Ciliary Neurotrophic Factor Receptor (CNTFR, Accession NM_001842), a gene which is critical for the developing nervous system. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTFR. The function of CNTFR has been established by previous studies. Davis et al. (1991) used the 'tagged-ligand panning' procedure to clone a receptor for ciliary neurotrophic factor (OMIM Ref. No. 118945). This receptor is expressed exclusively in the nervous system and skeletal muscle. The CNTF receptor was found to have a structure unrelated to the receptors utilized by the nerve growth factor family of neurotrophic molecules, but instead is most homologous to the receptor for a cytokine, interleukin-6 (IL6; 147620). This similarity suggested that the CNTF receptor, like the IL6 receptor, requires a second, signal-transducing component. In contrast to all known receptors, the CNTF receptor is anchored to cell membranes by a glycosylphosphatidylinositol linkage. Donaldson et al. (1993) mapped the CNTFR gene to chromosome 9 by PCR on a panel of human/CHO somatic cell hybrids and regional-

ized the assignment to 9p13 by PCR on a panel of radiation hybrids. By interspecific backcross linkage analysis, Pilz et al. (1995) mapped the *Cntfr* gene to mouse chromosome 4. By fluorescence in situ hybridization, Valenzuela et al. (1995) mapped the *CNTFR* gene to 9p13, and by interspecific backcross linkage analysis, they mapped the gene to mouse chromosome 4 in a region of known homology of synteny to 9p. Valenzuela et al. (1995) found that the human and mouse genes have an identical intron/exon structure that correlates well with the domain structure of the protein. The signal peptide and the immunoglobulin-like domain are each encoded by a single exon, the cytokine receptor-like domain is distributed among 4 exons, and the C-terminal glycosylphosphatidylinositol recognition domain is encoded by the final coding exon. The position of the introns within the cytokine receptor-like domain corresponds to that found in other members of the cytokine receptor superfamily.

[14108] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14109] Davis, S.; Aldrich, T. H.; Valenzuela, D. M.; Wong, V.; Furth, M. E.; Squinto, S. P.; Yancopoulos, G. D. : The re-

ceptor for ciliary neurotrophic factor. Science 253: 59–63, 1991. ; and

[14110] Pilz, A.; Woodward, K.; Povey, S.; Abbott, C. : Comparative mapping of 50 human chromosome 9 loci in the laboratory mouse. Genomics 25: 139–149, 1995.

[14111] Further studies establishing the function and utilities of CNTFR are found in John Hopkins OMIM database record ID 118946, and in cited publications numbered 1462, 146 and 1464 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Desmocollin 3 (DSC3, Accession NM_001941) is another VGAM230 host target gene. DSC3 BINDING SITE1 and DSC3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DSC3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSC3 BINDING SITE1 and DSC3 BINDING SITE2, designated SEQ ID:7654 and SEQ ID:23665 respectively, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14112] Another function of VGAM230 is therefore inhibition of Desmocollin 3 (DSC3, Accession NM_001941), a gene

which is a component of intercellular desmosome junctions. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSC3. The function of DSC3 has been established by previous studies. From a bladder carcinoma cell line cDNA library, Kawamura et al. (1994) cloned a human cDNA encoding for a novel transmembrane protein. Sequence analysis revealed an open reading frame of 2,691 bp encoding a protein of 896 amino acids. Sequence comparisons showed significant homology to desmocollins, intercellular adhesion molecules belonging to the cadherin superfamily. The protein consisted of a signal peptide of 30 amino acids, a precursor segment of 105 amino acids, and a mature protein of 761 amino acids. Antibodies recognizing the predicted mature adhesion molecule of the protein stained antigens along the cell boundaries of normal human keratinocytes resembling the pattern of desmosome localization. Kawamura et al. (1994) concluded that the clone represented a new member of the desmocollin family and tentatively referred to it as desmocollin type 4. King et al. (1995) used the designation DSC3 for a gene encoding a desmocollin present in human foreskin epidermis and stated that the

gene is identical to that encoding the desmocollin isolated from a bladder carcinoma cell line and called DSC4 by Kawamura et al. (1994). They likewise mapped the gene to chromosome 18 by PCR analysis of rodent/human somatic cell hybrids. They stated that the cDNA sequence showed 67% amino acid identity with the original human desmocollin, designated DSC2, and 52% amino acid identity with DSC1. By in situ hybridization studies, they showed that DSC1 was not present in any of the nonkeratinizing human epithelia, such as buccal mucosa, cervix, and esophagus, whereas all these internal epithelia expressed DSC2 and DSC3 and were present in most of the living layers of tissues, including the basal layers.

[14113] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14114] Kawamura, K.; Watanabe, K.; Suzuki, T.; Yamakawa, T.; Kamiyama, T.; Nakagawa, H.; Tsurufuji, S. : cDNA cloning and expression of a novel human desmocollin. J. Biol. Chem. 269: 26295–26302, 1994. ; and

[14115] King, I. A.; Sullivan, K. H.; Bennett, R., Jr.; Buxton, R. S. : The desmocollins of human foreskin epidermis: identification and chromosomal assignment of a third gene and ex-

pression p.

[14116] Further studies establishing the function and utilities of DSC3 are found in John Hopkins OMIM database record ID 600271, and in cited publications numbered 7347–7349 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protocadherin Alpha 9 (PCDHA9, Accession NM_014005) is another VGAM230 host target gene. PCDHA9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PCDHA9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHA9 BINDING SITE, designated SEQ ID:15209, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14117] Another function of VGAM230 is therefore inhibition of Protocadherin Alpha 9 (PCDHA9, Accession NM_014005), a gene which is a calcium-dependent cell-adhesion protein. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHA9. The function of PCDHA9 and its association with various diseases and clinical con-

ditions, has been established by previous studies, as described hereinabove with reference to VGAM71.RPP30 (Accession NM_006413) is another VGAM230 host target gene. RPP30 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPP30, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPP30 BINDING SITE, designated SEQ ID:13124, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14118] Another function of VGAM230 is therefore inhibition of RPP30 (Accession NM_006413), a gene which is a component of ribonuclease p that processes 5' ends of precursor tRNAs. Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPP30. The function of RPP30 has been established by previous studies. By biochemical purification of RNase P, micropeptide sequence analysis, and EST database searching, Eder et al. (1997) obtained a cDNA encoding RPP30. The deduced protein contains 268 amino acids with a predicted molecular mass of nearly 30

kD. Jarrous et al. (1998) determined that RPP30 is a target for antisera from systemic sclerosis patients. Immunoprecipitation analysis showed that polyclonal antibodies raised against RPP20, RPP30, RPP38, or RPP40 interact with RNase P from HeLa cells.

[14119] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14120] Eder, P. S.; Kekuda, R.; Stolc, V.; Altman, S. : Characterization of two scleroderma autoimmune antigens that copurify with human ribonuclease P. Proc. Nat. Acad. Sci. 94: 1101-1106, 1997. ; and

[14121] Jarrous, N.; Eder, P. S.; Guerrier-Takada, C.; Hoog, C.; Altman, S. : Autoantigenic properties of some protein subunits of catalytically active complexes of human ribonuclease P. RNA 4: 407.

[14122] Further studies establishing the function and utilities of RPP30 are found in John Hopkins OMIM database record ID 606115, and in cited publications numbered 74 and 897 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. AFAP (Accession NM_021638) is another VGAM230 host target gene. AFAP BINDING SITE is HOST TARGET binding site found in the

3` untranslated region of mRNA encoded by AFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AFAP BINDING SITE, designated SEQ ID:22291, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14123] Another function of VGAM230 is therefore inhibition of AFAP (Accession NM_021638). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AFAP. FLJ10583 (Accession NM_018148) is another VGAM230 host target gene. FLJ10583 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10583, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10583 BINDING SITE, designated SEQ ID:19950, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14124] Another function of VGAM230 is therefore inhibition of FLJ10583 (Accession NM_018148). Accordingly, utilities of

VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10583. FLJ20208 (Accession NM_017712) is another VGAM230 host target gene. FLJ20208 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20208, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20208 BINDING SITE, designated SEQ ID:19292, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14125] Another function of VGAM230 is therefore inhibition of FLJ20208 (Accession NM_017712). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20208. FLJ23519 (Accession NM_032240) is another VGAM230 host target gene. FLJ23519 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23519 BINDING SITE,

designated SEQ ID:25977, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14126] Another function of VGAM230 is therefore inhibition of FLJ23519 (Accession NM_032240). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23519. TADA3L (Accession NM_133480) is another VGAM230 host target gene. TADA3L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TADA3L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TADA3L BINDING SITE, designated SEQ ID:28548, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14127] Another function of VGAM230 is therefore inhibition of TADA3L (Accession NM_133480). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TADA3L. Ubiquitin Specific Protease 24 (USP24, Accession XM_165973) is another VGAM230 host target gene. USP24

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP24 BINDING SITE, designated SEQ ID:43817, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14128] Another function of VGAM230 is therefore inhibition of Ubiquitin Specific Protease 24 (USP24, Accession XM_165973). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP24. LOC118987 (Accession XM_058361) is another VGAM230 host target gene. LOC118987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC118987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118987 BINDING SITE, designated SEQ ID:36607, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14129] Another function of VGAM230 is therefore inhibition of LOC118987 (Accession XM_058361). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118987. LOC138046 (Accession XM_059936) is another VGAM230 host target gene. LOC138046 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC138046, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138046 BINDING SITE, designated SEQ ID:37115, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14130] Another function of VGAM230 is therefore inhibition of LOC138046 (Accession XM_059936). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138046. LOC147178 (Accession XM_028755) is another VGAM230 host target gene. LOC147178 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147178, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147178 BINDING SITE, designated SEQ ID:30742, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14131] Another function of VGAM230 is therefore inhibition of LOC147178 (Accession XM_028755). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147178. LOC147991 (Accession XM_085993) is another VGAM230 host target gene. LOC147991 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147991, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147991 BINDING SITE, designated SEQ ID:38436, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14132] Another function of VGAM230 is therefore inhibition of LOC147991 (Accession XM_085993). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC147991. LOC155434 (Accession XM_098723) is another VGAM230 host target gene. LOC155434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155434 BINDING SITE, designated SEQ ID:41771, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14133] Another function of VGAM230 is therefore inhibition of LOC155434 (Accession XM_098723). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155434. LOC199699 (Accession XM_113990) is another VGAM230 host target gene. LOC199699 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199699, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199699 BINDING SITE, designated SEQ ID:42597, to the nucleotide sequence of VGAM230 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2941.

[14134] Another function of VGAM230 is therefore inhibition of LOC199699 (Accession XM_113990). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199699. LOC93048 (Accession XM_048903) is another VGAM230 host target gene. LOC93048 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC93048, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93048 BINDING SITE, designated SEQ ID:35295, to the nucleotide sequence of VGAM230 RNA, herein designated VGAM RNA, also designated SEQ ID:2941.

[14135] Another function of VGAM230 is therefore inhibition of LOC93048 (Accession XM_048903). Accordingly, utilities of VGAM230 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93048. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 231 (VGAM231) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14136] VGAM231 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM231 was detected is described hereinabove with reference to Figs. 1–8.

[14137] VGAM231 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14138] VGAM231 gene encodes a VGAM231 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM231 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM231 precursor RNA is designated SEQ ID:217, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:217 is located at position 73231 relative to the genome of Callitrichine Herpesvirus 3.

[14139] VGAM231 precursor RNA folds onto itself, forming

VGAM231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14140] An enzyme complex designated DICER COMPLEX, `dices` the VGAM231 folded precursor RNA into VGAM231 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM231 RNA is designated SEQ ID:2942, and is provided hereinbelow with reference to the sequence listing part.

[14141] VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM231 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14142] VGAM231 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM231 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM231 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14143] The complementary binding of VGAM231 RNA, herein designated VGAM RNA, to host target binding sites on VGAM231 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM231 host target RNA into VGAM231 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14144] It is appreciated that VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM231 host target genes. The mRNA of each one of this plurality of VGAM231 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM231 RNA, herein designated VGAM RNA, and which when bound by VGAM231 RNA causes inhibition of translation of respective one or more VGAM231 host target proteins.

[14145] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM231 gene, herein designated VGAM GENE, on one or more VGAM231 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14146] It is yet further appreciated that a function of VGAM231 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM231 correlate with, and may be deduced from, the identity of the host target genes which VGAM231 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[14147] Nucleotide sequences of the VGAM231 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM231 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM231 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM231 are further described hereinbelow with reference to Table 1.

[14148] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM231 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM231 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14149] As mentioned hereinabove with reference to Fig. 1, a function of VGAM231 gene, herein designated VGAM is inhibition of expression of VGAM231 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM231 correlate with, and may be deduced from, the identity of the target genes which VGAM231 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[14150] Amyloid Beta (A4) Precursor-like Protein 2 (APLP2, Accession XM_165592) is a VGAM231 host target gene. APLP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APLP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APLP2 BINDING SITE, designated SEQ ID:43699, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14151] A function of VGAM231 is therefore inhibition of Amyloid Beta (A4) Precursor-like Protein 2 (APLP2, Accession XM_165592), a gene which may play a role in the regulation of hemostasis. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APLP2. The function of APLP2 has been established by previous studies. Yan et al. (1990) cloned a cDNA that encoded a human sperm membrane protein identified by a monoclonal antibody raised against this protein and designated YWK-II. They found that the deduced polypeptide contains a segment with high homology to the transmembrane-cytoplasmic do-

mains of the A4 amyloid protein (APP; 104760) found in brain plaques of Alzheimer disease patients. Rather than the lys-lys-lys sequence found in the A4 protein, an arg-lys-arg sequence was found at the probable membrane-cytoplasmic junction that may represent a unique property of sperm membrane proteins. The human amyloid precursor-like protein APLP2 is a highly conserved homolog of a sequence-specific DNA-binding mouse protein with an important function in the cell cycle. The mouse amyloid precursor-like protein Aplp1 has 42% sequence identity to mouse App; the human homolog of APLP1 (OMIM Ref. No. 104775) maps to 19q11-q13.2 (Wasco et al., 1993). By study of somatic cell hybrids segregating human chromosomes, von der Kammer et al. (1994) mapped the APLP2 gene to chromosome 11; by fluorescence in situ hybridization, the assignment was confirmed and further localized to 11q23-q25. By FISH, Leach et al. (1999) mapped the gene to 11q24.

[14152] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14153] Wasco, W.; Brook, J. D.; Tanzi, R. E. : The amyloid precursor-like protein (APLP) gene maps to the long arm of hu-

- man chromosome 19. Genomics 15: 237–239, 1993. ; and
- [14154] Yan, Y. C.; Bai, Y.; Wang, L.; Miao, S.; Koide, S. S. : Characterization of cDNA encoding a human sperm membrane protein related to A4 amyloid protein. Proc. Nat. Acad. Sci. 87: 2405–240.
- [14155] Further studies establishing the function and utilities of APLP2 are found in John Hopkins OMIM database record ID 104776, and in cited publications numbered 4310–4312, 430 and 4313–4314 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Apical Protein–like (*Xenopus laevis*) (APXL, Accession NM_001649) is another VGAM231 host target gene. APXL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by APXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APXL BINDING SITE, designated SEQ ID:7351, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.
- [14156] Another function of VGAM231 is therefore inhibition of Apical Protein–like (*Xenopus laevis*) (APXL, Accession NM_001649), a gene which is implicated in amiloride–sen–

sitive sodium channel activity. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APXL. The function of APXL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152. Collagen, Type I, Alpha 2 (COL1A2, Accession NM_000089) is another VGAM231 host target gene. COL1A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL1A2 BINDING SITE, designated SEQ ID:5542, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14157] Another function of VGAM231 is therefore inhibition of Collagen, Type I, Alpha 2 (COL1A2, Accession NM_000089). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL1A2. Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession

NM_000150) is another VGAM231 host target gene. FUT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT6 BINDING SITE, designated SEQ ID:5651, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14158] Another function of VGAM231 is therefore inhibition of Fucosyltransferase 6 (alpha (1,3) Fucosyltransferase) (FUT6, Accession NM_000150), a gene which is involved in the biosynthesis of the e-selectin ligand, sialyl-lewis x. catalyzes the transfer of fucose from gdp- beta-fucose to alpha-2,3 sialylated substrates. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT6. The function of FUT6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM194.JJAZ1 (Accession NM_015355) is another VGAM231 host target gene. JJAZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by JJAZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JJAZ1 BINDING SITE, designated SEQ ID:17654, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14159] Another function of VGAM231 is therefore inhibition of JJAZ1 (Accession NM_015355), a gene which is a zinc finger protein. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JJAZ1. The function of JJAZ1 has been established by previous studies. Nagase et al. (1995) deduced the sequence of a full-length cDNA clone from cell line KG-1, which they designated KIAA0160, encoding a predicted 803-amino acid protein. Northern blot analysis revealed expression in all tissues tested. A variety of cytogenetic abnormalities involving chromosome 7 have been reported in endometrial stromal sarcomas, including a recurrent t(7;17)(p15;q21). Koontz et al. (2001) identified 2 zinc finger genes, which they termed JAZF1 (OMIM Ref. No. 606246) and JJAZ1, at the sites of the 7p15 and 17q21 breakpoints, respectively. Analyses of

tumor RNA indicated that a JAZF1/JJAZ1 fusion was present in all types of endometrial stromal tumors; however, the fusion appeared to be rarer among endometrial stromal sarcomas that would be considered high-grade according to certain classification schemes

[14160] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14161] Koontz, J. I.; Soreng, A. L.; Nucci, M.; Kuo, F. C.; Pauwels, P.; van den Berghe, H.; Cin, P. D.; Fletcher, J. A.; Sklar, J. : Frequent fusion of the JAZF1 and JJAZ1 genes in endometrial stromal tumors. Proc. Nat. Acad. Sci. 98: 6348–6353, 2001. ; and

[14162] Nagase, T.; Seki, N.; Tanaka, A.; Ishikawa, K.; Nomura, N. : Prediction of the coding sequences of unidentified human genes. IV. The coding sequences of 40 new genes (KIAA0121–KIAA0160).

[14163] Further studies establishing the function and utilities of JJAZ1 are found in John Hopkins OMIM database record ID 606245, and in cited publications numbered 613 and 10969 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor-type, Z Polypeptide 1

(PTPRZ1, Accession NM_002851) is another VGAM231 host target gene. PTPRZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTPRZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRZ1 BINDING SITE, designated SEQ ID:8745, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14164] Another function of VGAM231 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor-type, Z Polypeptide 1 (PTPRZ1, Accession NM_002851), a gene which may be involved in the regulation of specific developmental processes in the CNS. Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRZ1. The function of PTPRZ1 has been established by previous studies. Phosphorylation of proteins on tyrosine residues plays a key role in the signaling of cell growth, differentiation, and transformation. The net phosphorylation of cellular proteins on tyrosine residues is controlled by the balanced action of protein-tyrosine kinases and protein-tyrosine

phosphatases present in the cell. Levy et al. (1993) isolated cDNA clones and deduced the complete amino acid sequence of a large receptor-type protein tyrosine phosphatase containing 2,307 amino acids. They found that the protein, designated PTP-zeta (PTPRZ), is a transmembrane protein with 2 cytoplasmic PTPase domains and a 1,616-amino acid extracellular domain. As in PTP-gamma (OMIM Ref. No. 176886), the 266 N-terminal residues of the extracellular domain are homologous to carbonic anhydrases (see OMIM Ref. No. 114880). The human gene encoding PTPRZ was mapped to chromosome 7 by analysis of rodent-human hybrids and was regionalized to 7q31.3-q32 by chromosomal in situ hybridization. Northern blot analysis showed that PTP-zeta is expressed only in the central nervous system. By in situ hybridization, Levy et al. (1993) localized the expression to different regions of the adult brain, including the Purkinje cell layer of the cerebellum, the dentate gyrus, and the subependymal layer of the anterior horn of the lateral ventricle. They stated that this was the first mammalian tyrosine phosphatase whose expression is restricted to the nervous system. High levels of expression in the embryonic brain suggested an important role in CNS development. Ariyama

et al. (1995) localized the PTPRZ gene to 7q31.3 by somatic cell hybrid mapping and fluorescence in situ hybridization. Animal model experiments lend further support to the function of PTPRZ1. Harroch et al. (2002) examined the susceptibility of mice deficient in Pprz to experimental autoimmune encephalomyelitis (EAE), a model of multiple sclerosis (OMIM Ref. No. 126200). They observed that mice deficient in Ptporz showed impaired recovery from EAE induced by myelin-oligodendrocyte glycoprotein (MOG; 159465) peptide. This sustained paralysis was associated with increased apoptosis of mature oligodendrocytes in the spinal cords of mutant mice at the peak of inflammation. They further demonstrated that expression of PTPRZ1, the human homolog, is induced in multiple sclerosis lesions and that the gene is specifically expressed in remyelinating oligodendrocytes in these lesions. These reports support a role for Ptporz in oligodendrocyte survival and in recovery from demyelinating disease.

[14165] It is appreciated that the abovementioned animal model for PTPRZ1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

- [14166] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [14167] Ariyama, T.; Hasegawa, K.; Inazawa, J.; Mizuno, K.; Ogi-moto, M.; Katagiri, T.; Yakura, H. : Assignment of the human protein tyrosine phosphatase, receptor-type, zeta (PTPRZ) gene to chromosome band 7q31.3. *Cytogenet. Cell Genet.* 70: 52–54, 1995. ; and
- [14168] Harroch, S.; Furtado, G. C.; Brueck, W.; Rosenbluth, J.; Lafaille, J.; Chao, M.; Buxbaum, J. D.; Schlessinger, J. : A critical role for the protein tyrosine phosphatase receptor type Z i.
- [14169] Further studies establishing the function and utilities of PTPRZ1 are found in John Hopkins OMIM database record ID 176891, and in cited publications numbered 1058 and 11262 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Rho Guanine Nucleotide Exchange Factor (GEF) 15 (ARHGEF15, Accession NM_014958) is another VGAM231 host target gene. ARHGEF15 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARHGEF15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF15 BINDING SITE, designated SEQ ID:17316, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14170] Another function of VGAM231 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 15 (ARHGEF15, Accession NM_014958). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF15. Death Associated Transcription Factor 1 (DATF1, Accession NM_022105) is another VGAM231 host target gene. DATF1 BINDING SITE1 and DATF1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DATF1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DATF1 BINDING SITE1 and DATF1 BINDING SITE2, designated SEQ ID:22651 and SEQ ID:28062 respectively, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14171] Another function of VGAM231 is therefore inhibition of

Death Associated Transcription Factor 1 (DATF1, Accession NM_022105). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DATF1. DKFZp761B0514 (Accession NM_032289) is another VGAM231 host target gene. DKFZp761B0514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B0514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B0514 BINDING SITE, designated SEQ ID:26051, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14172] Another function of VGAM231 is therefore inhibition of DKFZp761B0514 (Accession NM_032289). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B0514. Family with Sequence Similarity 3, Member C (FAM3C, Accession NM_014888) is another VGAM231 host target gene. FAM3C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by FAM3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAM3C BINDING SITE, designated SEQ ID:17039, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14173] Another function of VGAM231 is therefore inhibition of Family with Sequence Similarity 3, Member C (FAM3C, Accession NM_014888). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAM3C. FLJ20337 (Accession NM_017772) is another VGAM231 host target gene. FLJ20337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20337 BINDING SITE, designated SEQ ID:19394, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14174] Another function of VGAM231 is therefore inhibition of

FLJ20337 (Accession NM_017772). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20337. Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM_032664) is another VGAM231 host target gene. FUT10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FUT10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FUT10 BINDING SITE, designated SEQ ID:26393, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14175] Another function of VGAM231 is therefore inhibition of Fucosyltransferase 10 (alpha (1,3) Fucosyltransferase) (FUT10, Accession NM_032664). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FUT10. HEF1 (Accession NM_006403) is another VGAM231 host target gene. HEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEF1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEF1 BINDING SITE, designated SEQ ID:13112, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14176] Another function of VGAM231 is therefore inhibition of HEF1 (Accession NM_006403). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEF1. KIAA0903 (Accession XM_049251) is another VGAM231 host target gene. KIAA0903 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0903, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0903 BINDING SITE, designated SEQ ID:35367, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14177] Another function of VGAM231 is therefore inhibition of KIAA0903 (Accession XM_049251). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0903. MBLL39 (Accession NM_144778) is another VGAM231 host target gene. MBLL39 BINDING SITE1 and MBLL39 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MBLL39, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBLL39 BINDING SITE1 and MBLL39 BINDING SITE2, designated SEQ ID:29577 and SEQ ID:12320 respectively, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14178] Another function of VGAM231 is therefore inhibition of MBLL39 (Accession NM_144778). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBLL39. LOC145241 (Accession XM_031799) is another VGAM231 host target gene. LOC145241 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145241, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC145241 BINDING SITE, designated SEQ ID:31483, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14179] Another function of VGAM231 is therefore inhibition of LOC145241 (Accession XM_031799). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145241. LOC157503 (Accession XM_098767) is another VGAM231 host target gene. LOC157503 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157503 BINDING SITE, designated SEQ ID:41811, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14180] Another function of VGAM231 is therefore inhibition of LOC157503 (Accession XM_098767). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157503. LOC163231 (Accession XM_092094) is an-

other VGAM231 host target gene. LOC163231 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163231 BINDING SITE, designated SEQ ID:40094, to the nucleotide sequence of VGAM231 RNA, herein designated VGAM RNA, also designated SEQ ID:2942.

[14181] Another function of VGAM231 is therefore inhibition of LOC163231 (Accession XM_092094). Accordingly, utilities of VGAM231 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163231. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 232 (VGAM232) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14182] VGAM232 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM232 was detected is described

hereinabove with reference to Figs. 1–8.

[14183] VGAM232 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14184] VGAM232 gene encodes a VGAM232 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM232 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM232 precursor RNA is designated SEQ ID:218, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:218 is located at position 121062 relative to the genome of Callitrichine Herpesvirus 3.

[14185] VGAM232 precursor RNA folds onto itself, forming VGAM232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14186] An enzyme complex designated DICER COMPLEX, `dices` the VGAM232 folded precursor RNA into VGAM232 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM232 RNA is designated SEQ ID:2943, and is provided hereinbelow with reference to the sequence listing part.

[14187] VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM232 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14188] VGAM232 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM232 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM232 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM232 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14189] The complementary binding of VGAM232 RNA, herein designated VGAM RNA, to host target binding sites on VGAM232 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM232 host target RNA into VGAM232 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14190] It is appreciated that VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM232 host target genes. The mRNA of each one of this plurality of VGAM232 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM232 RNA, herein designated VGAM RNA, and which when bound by VGAM232 RNA causes inhibition of translation of respective one or more VGAM232 host target proteins.

[14191] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM232 gene, herein designated VGAM GENE, on one or more VGAM232 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14192] It is yet further appreciated that a function of VGAM232 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM232 correlate with, and may be deduced from, the identity of the host target genes which VGAM232 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14193] Nucleotide sequences of the VGAM232 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM232 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM232 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM232 are further described hereinbelow with reference to Table 1.

[14194] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM232 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM232 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14195] As mentioned hereinabove with reference to Fig. 1, a function of VGAM232 gene, herein designated VGAM is inhibition of expression of VGAM232 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM232 correlate with, and may be deduced from, the identity of the target genes which VGAM232 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14196] Arylsulfatase D (ARSD, Accession NM_009589) is a VGAM232 host target gene. ARSD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARSD BINDING SITE, designated SEQ ID:14317, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14197] A function of VGAM232 is therefore inhibition of Arylsulfatase D (ARSD, Accession NM_009589), a gene which hydrolyzes sulfate groups from sugar residues in complex glycoconjugates. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARSD. The function of ARSD has been established by previous studies. In the course of positional cloning of the gene mutant in X-linked chondrodysplasia punctata (OMIM Ref. No. 302950), Franco et al. (1995) identified a cluster of 3 sulfatase genes located in the region Xp22.3. The genes were arylsulfatases and were designated ARSD, ARSE (OMIM Ref. No. 300180), and ARSF (OMIM Ref. No. 300003), in that order, proceeding from the telomere of Xp toward the centromere. Mutations in ARSE were identified in males with chondrodysplasia punctata. Franco et al. (1995) showed that both ARSD and ARSE have 11 exons and are transcribed toward the telomere. Their natural substrate

was not determined. Meroni et al. (1996) reported that ARSD and ARSE have several typical features of genes that map in the pseudoautosomal region of the X chromosome, i.e., they escape X inactivation, have homologs on the Y chromosome, and are not conserved in mouse.

Meroni et al. (1996) noted that ARSD, ARSE, and STS have a conserved gene structure; alignment of the genomic structures revealed perfect conservation of the intron-exon junctions. Sequence analysis of the Y-linked homologs of ARSD and ARSE indicated that they represent truncated pseudogenes.

[14198] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14199] Franco, B.; Meroni, G.; Parenti, G.; Levilliers, J.; Bernard, L.; Gebbia, M.; Cox, L.; Maroteaux, P.; Sheffield, L.; Rappold, G. A.; Andria, G.; Petit, C.; Ballabio, A. : A cluster of sulfatase genes on Xp22.3: mutations in chondrodysplasia punctata (CDPX) and implications for warfarin embryopathy. Cell 81: 1-20, 1995. ; and

[14200] Meroni, G.; Franco, B.; Archidiacono, N.; Messali, S.; Andolfi, G.; Rocchi, M.; Ballabio, A. : Characterization of a cluster of sulfatase genes on Xp22.3 suggests gene dupli-

cations in a.

[14201] Further studies establishing the function and utilities of ARSD are found in John Hopkins OMIM database record ID 300002, and in cited publications numbered 9009–9010 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519) is another VGAM232 host target gene. BRF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BRF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BRF1 BINDING SITE, designated SEQ ID:7258, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14202] Another function of VGAM232 is therefore inhibition of BRF1 Homolog, Subunit of RNA Polymerase III Transcription Initiation Factor IIIB (*S. cerevisiae*) (BRF1, Accession NM_001519), a gene which is a general activator of RNA polymerase III. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with BRF1. The function of BRF1 has been established by previous studies. By screening a Burkitt lymphoma and other human cDNA cell libraries using degenerate PCR primers corresponding to peptide sequences of the 90-kD subunit of GTF3B, Wang and Roeder (1995) obtained a cDNA encoding TAF3B2, which they called TFIIIB90. Sequence analysis revealed that the 675-amino acid TAF3B2 protein contains a high mobility group protein-2 (HMG2; 163906)-related region in the highly charged C-terminal half of the protein and a sequence related to GTF2B (OMIM Ref. No. 189963) in the N terminus. Western blot analysis showed that TAF3B2 is expressed as a 92-kD protein, the C terminus of which binds TBP. Recombinant TAF3B2 together with TBP, but neither alone, could replace purified natural GTF3B. Deletion of either the N-terminal GTF2B-related or the C-terminal HMG2-related half of the protein abolished activity. Mital et al. (1996) cloned a cDNA identical to the TAF3B2 cDNA obtained by Wang and Roeder (1995) except for scattered nucleotide differences and the presence of 6 additional nucleotides. These last differences change the open reading frame, predicting a different sequence over 67 amino acids of the TAF3B2 protein, which Mital et

al. (1996) called BRF due to its homology with the *S. cerevisiae* BRF protein. Mital et al. (1996) confirmed the association of TAF3B2 with TBP reported by Wang and Roeder (1995).

[14203] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14204] Wang, Z.; Roeder, R. G. : Structure and function of a human transcription factor TFIIB subunit that is evolutionarily conserved and contains both TFIIB- and high-mobility-group protein 2-related domains. *Proc. Nat. Acad. Sci.* 92: 7026-7030, 1995. ; and

[14205] Mital, R.; Kobayashi, R.; Hernandez, N. : RNA polymerase III transcription from the human U6 and adenovirus type 2 VAI promoters has different requirements for human BRF, a subunit of hu.

[14206] Further studies establishing the function and utilities of BRF1 are found in John Hopkins OMIM database record ID 604902, and in cited publications numbered 2908-2909 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 3 (DDX3, Accession NM_024005) is another VGAM232 host target gene.

DDX3 BINDING SITE1 and DDX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DDX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX3 BINDING SITE1 and DDX3 BINDING SITE2, designated SEQ ID:23433 and SEQ ID:7037 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14207] Another function of VGAM232 is therefore inhibition of DEAD/H (Asp–Glu–Ala–Asp/His) Box Polypeptide 3 (DDX3, Accession NM_024005), a gene which interacts with hepatitis c virus core protein resulting a change in intracellular location. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX3. The function of DDX3 has been established by previous studies. DEAD box proteins are putative RNA helicases that have a characteristic Asp–Glu–Ala–Asp (DEAD) box as 1 of 8 highly conserved sequence motifs. See 600396. Chung et al. (1995) cloned cDNAs encoding DDX3 (Genbank U50553), a putative RNA helicase belonging to the DEAD box protein family. Lahn

and Page (1997) identified DDX3, which they called DBX, as 1 of 5 X-linked genes that have homologs located in the nonrecombining region of the Y chromosome (NRY). See DBY (OMIM Ref. No. 400010). They determined that these 5 X-linked genes escape X inactivation. Lahn and Page (1997) postulated that these 5 genes are cases in which gene expression is maintained at comparable levels in males and females by preservation of homologous genes on both the X and the NRY, with male and female cells expressing both copies of each gene. Sequence analysis revealed that DBX shares 91% protein sequence identity with DBY, the Y-linked homolog.

[14208] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14209] Lahn, B. T.; Page, D. C. : Functional coherence of the human Y chromosome. *Science* 278: 675–680, 1997. ; and

[14210] Park, S. H.; Lee, S.-G.; Kim, Y.; Song, K. : Assignment of a human putative RNA helicase gene, DDX3, to human X chromosome bands p11.3–p11.23. *Cytogenet. Cell Genet.* 81: 178–179, 1998.

[14211] Further studies establishing the function and utilities of DDX3 are found in John Hopkins OMIM database record ID

300160, and in cited publications numbered 1099 and 11000 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Engrailed Homolog 2 (EN2, Accession NM_001427) is another VGAM232 host target gene. EN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EN2 BINDING SITE, designated SEQ ID:7145, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14212] Another function of VGAM232 is therefore inhibition of Engrailed Homolog 2 (EN2, Accession NM_001427), a gene which may be required for normal cerebellar development; a homeobox protein, very strongly similar to murine En2. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EN2. The function of EN2 has been established by previous studies. In *Drosophila*, the 'engrailed' (en) homeo box protein plays an important role during development in segmentation, where it is required

for the formation of posterior compartments. See EN1 (OMIM Ref. No. 131290). By low stringency hybridization, Poole et al. (1989) isolated from a human cosmid genomic library sequences homologous with a probe from the *Drosophila* 'engrailed' gene. Partial nucleotide sequence analysis showed a consensus splice acceptor site followed by an open reading frame capable of coding 104 amino acids; the first 94 amino acids showed 71% identity with the *Drosophila* engrailed protein. The shared region contained a homeo domain. At the amino acid level, the human sequence was 85% identical with the mouse En1 gene and 100% identical with the mouse En2 gene. Logan et al. (1992) isolated human and chicken genomic clones of the EN1 and EN2 genes. As in mouse, the predicted coding region of the human and chicken EN2 genes is interrupted by a single intron. The deduced 333-amino acid human EN2 protein is 90% identical to mouse En1. By sequence analysis, the authors determined that En proteins from various species contain 5 distinct conserved subregions. Northern blot analysis revealed that EN2, but not EN1, is expressed as a 4-kb mRNA in human cerebellum. Similarly, Western blots indicated that only EN2 is expressed fetal cerebellum. To study the role of the En2 gene in de-

velopment, Joyner et al. (1989) created mutations in 3 pluripotent embryonic stem cell (ES) lines by homologous recombination. Joyner et al. (1991) generated mice homozygous for a targeted deletion of the En2 homeo box. The mutant mice were viable and showed no obvious defects in embryonic development. The authors suggested that this might be due to functional redundancy of En2 and En1. They found that the mutant mice had abnormal foliation in the adult cerebellum, where normally only En2 is expressed. To determine whether the contrasting phenotypes of En2 and En1 reflect differences in temporal expression or biochemical activity of the En proteins, Hanks et al. (1995) replaced En1 coding sequences with En2 sequences in transgenic mice by gene targeting. The En2 sequences rescued all En1 mutant defects, demonstrating that the difference between En1 and En2 stems from their divergent expression patterns. By Southern blot analysis of DNA from a panel of human-hamster somatic cell hybrids, Poole et al. (1989) mapped the EN2 gene to human chromosome 7; regional mapping by in situ hybridization localized it to 7q36. Logan et al. (1989) arrived independently at the same assignment.

[14213] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [14214] Hanks, M.; Wurst, W.; Anson–Cartwright, L.; Auerbach, A. B.; Joyner, A. L. : Rescue of the En–1 mutant phenotype by replacement of En–1 with En–2. Science 269: 679–682, 1995. ; and
- [14215] Joyner, A. L.; Herrup, K.; Auerbach, B. A.; Davis, C. A.; Rossant, J. : Subtle cerebellar phenotype in mice homozygous for a targeted deletion of the En–2 homeobox. Science 251: 1239–124.
- [14216] Further studies establishing the function and utilities of EN2 are found in John Hopkins OMIM database record ID 131310, and in cited publications numbered 2603, 2977–2978, 2606–260 and 2979 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Growth Arrest–specific 7 (GAS7, Accession NM_003644) is another VGAM232 host target gene. GAS7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by GAS7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS7 BINDING SITE, designated SEQ ID:9716,

to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14217] Another function of VGAM232 is therefore inhibition of Growth Arrest-specific 7 (GAS7, Accession NM_003644), a gene which may play a role in promoting maturation and morphological differentiation of cerebellar neurons. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS7. The function of GAS7 has been established by previous studies. Growth arrest-specific (GAS) genes are expressed preferentially in cells that enter a quiescent state. Ju et al. (1998) described the isolation and characterization of a GAS gene (GAS7) that is expressed primarily in vivo in terminally differentiated brain cells and particularly prominently in mature cerebellar Purkinje neurons. The gene had originally been identified in serum-starved murine fibroblasts. GAS7 transcripts encode a 48-kD protein containing a structural domain that resembles sequences of OCT2 (OMIM Ref. No. 602608), a POU transcription factor implicated in neuronal development, and synapsins, e.g., synapsin I (SYN1; 313440), which have a role in modulating neurotransmitter release. Using in situ hybridization and immunocytochemical anal-

ysis, Ju et al. (1998) showed that inhibition of production of GAS7 in terminally differentiating cultures of embryonic murine cerebellum impedes neurite outgrowth from maturing Purkinje cells. Conversely, GAS7 overexpression in undifferentiated neuroblastoma cell cultures dramatically promotes neurite-like outgrowth. Collectively, the results provided evidence for an association between expression of GAS7 and neuronal development. By analysis of cell hybrid DNAs prepared from a panel of 21 Chinese hamster/mouse hybrid cell lines, Ju et al. (1998) mapped the mouse Gas7 gene to chromosome 11. They reported that a human DNA fragment (GenBank G13706) having 85% sequence identity with Gas7 mapped to 17p, which is largely syngeneic with mouse chromosome 11 (Kurtz and Zimmer, 1995).

[14218] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14219] Ju, Y.-T.; Chang, A. C. Y.; She, B.-R.; Tsaur, M.-L.; Hwang, H.-M.; Chao, C. C.-K.; Cohen, S. N.; Lin-Chao, S. : Gas7: a gene expressed preferentially in growth-arrested fibroblasts and terminally differentiated Purkinje neurons affects neurite formation. Proc. Nat. Acad. Sci. 95: 11423-11428,

1998. ; and

[14220] Kurtz, A.; Zimmer, A. : Interspecies fluorescence in situ hybridization further defines syntenic homology between mouse chromosome 11 and human chromosome 17.

Mammalian Genome 6: 379–380.

[14221] Further studies establishing the function and utilities of GAS7 are found in John Hopkins OMIM database record ID 603127, and in cited publications numbered 641–64 and 644 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM_002084) is another VGAM232 host target gene. GPX3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPX3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPX3 BINDING SITE, designated SEQ ID:7879, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14222] Another function of VGAM232 is therefore inhibition of Glutathione Peroxidase 3 (plasma) (GPX3, Accession NM_002084), a gene which reduces lipid hydroperoxide

and H₂O₂ in plasma. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPX3. The function of GPX3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM225. Kelch-like 1 (Drosophila) (KLHL1, Accession NM_020866) is another VGAM232 host target gene. KLHL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KLHL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL1 BINDING SITE, designated SEQ ID:21919, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14223] Another function of VGAM232 is therefore inhibition of Kelch-like 1 (Drosophila) (KLHL1, Accession NM_020866). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL1. Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession

NM_015166) is another VGAM232 host target gene. MLC1 BINDING SITE1 and MLC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MLC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLC1 BINDING SITE1 and MLC1 BINDING SITE2, designated SEQ ID:17525 and SEQ ID:29219 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14224] Another function of VGAM232 is therefore inhibition of Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_015166). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLC1. Neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease) (NF1, Accession NM_000267) is another VGAM232 host target gene. NF1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of NF1 BINDING SITE, designated SEQ ID:5813, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14225] Another function of VGAM232 is therefore inhibition of Neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease) (NF1, Accession NM_000267). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NF1. Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531) is another VGAM232 host target gene. NTSR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTSR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTSR1 BINDING SITE, designated SEQ ID:8370, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14226] Another function of VGAM232 is therefore inhibition of Neurotensin Receptor 1 (high affinity) (NTSR1, Accession NM_002531), a gene which is associated with G proteins

that activate a phosphatidylinositol– calcium second messenger system. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTSR1. The function of NTSR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Protein Kinase C-like 1 (PRKCL1, Accession XM_031273) is another VGAM232 host target gene. PRKCL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRKCL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKCL1 BINDING SITE, designated SEQ ID:31329, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14227] Another function of VGAM232 is therefore inhibition of Protein Kinase C-like 1 (PRKCL1, Accession XM_031273). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKCL1. RAD52 Homolog (*S. cerevisiae*)

(RAD52, Accession NM_134422) is another VGAM232 host target gene. RAD52 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAD52, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAD52 BINDING SITE, designated SEQ ID:28645, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14228] Another function of VGAM232 is therefore inhibition of RAD52 Homolog (*S. cerevisiae*) (RAD52, Accession NM_134422). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAD52. Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM_004560) is another VGAM232 host target gene. ROR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROR2 BINDING SITE, designated SEQ ID:10899, to the nu-

cleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14229] Another function of VGAM232 is therefore inhibition of Receptor Tyrosine Kinase-like Orphan Receptor 2 (ROR2, Accession NM_004560), a gene which may be involved in the early formayion of the chonrocytes. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROR2. The function of ROR2 has been established by previous studies. Receptor tyrosine kinases often have critical roles in particular cell lineages by initiating signal cascades in those lineages. Many lineage-restricted receptor tyrosine kinases were initially identified as 'orphans' homologous to known receptors, and only subsequently used to identify their unknown growth factors. DeChiara et al. (2000) identified one such orphan, encoded by Ror2. They reported that disruption of mouse Ror2 leads to profound skeletal abnormalities, with essentially all endochondrally derived bones foreshortened or misshapen, albeit to differing degrees. Further, they found that Ror2 is selectively expressed in the chondrocytes of all developing cartilage anlagen, where it is essential during initial growth and patterning, as well as subsequently in the

proliferating chondrocytes of mature growth plates, where it is required for normal expansion. Thus, Ror2 encodes a receptor-like tyrosine kinase that is selectively expressed in, and particularly important for, the chondrocyte lineage. Animal model experiments lend further support to the function of ROR2. Takeuchi et al. (2000) generated mice with a mutation in the Ror2 gene and observed that homozygous mutant mice died just after birth, exhibiting dwarfism, severe cyanosis, and short limbs and tails.

Whole-mount in situ hybridization analysis showed that Ror2 is expressed in the branchial arches, heart, and limb/tailbuds, in addition to the developing nervous system. The Ror2-deficient mice had cardiac septal defects and skeletal abnormalities, including shorter limbs, vertebrae, and facial structure, with a particular defect in their distal portions. Takeuchi et al. (2000) concluded that Ror2 plays essential roles in the development of the heart and in limb/tail formation, in particular cardiac septal formation and ossification of distal portions of limbs and tails.

[14230] It is appreciated that the abovementioned animal model for ROR2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14231] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14232] Takeuchi, S.; Takeda, K.; Oishi, I.; Nomi, M.; Ikeya, M.; Itoh, K.; Tamura, S.; Ueda, T.; Hatta, T.; Otani, H.; Terashima, T.; Takada, S.; Yamamura, H.; Akira, S.; Minami, Y. : Mouse Ror2 receptor tyrosine kinase is required for the heart development and limb formation. *Genes Cells* 5: 71–78, 2000. ; and

[14233] DeChiara, T. M.; Kimble, R. B.; Poueymirou, W. T.; Rojas, J.; Masiakowski, P.; Valenzuela, D. M.; Yancopoulos, G. D. : Ror2, encoding a receptor–like tyrosine kinase, is required for carti.

[14234] Further studies establishing the function and utilities of ROR2 are found in John Hopkins OMIM database record ID 602337, and in cited publications numbered 6739, 12054, 2780–2781, 6013, 6310, 4678, 4846–278 and 6740 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine (or cysteine) Proteinase Inhibitor, Clade E (nexin, plasminogen activator inhibitor type 1), Member 2 (SERPINE2, Accession XM_059422) is another VGAM232 host target gene. SERPINE2 BINDING SITE is HOST TARGET binding site found in

the 5' untranslated region of mRNA encoded by SERPINE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINE2 BINDING SITE, designated SEQ ID:36988, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14235] Another function of VGAM232 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade E (nexin, plasminogen activator inhibitor type 1), Member 2 (SERPINE2, Accession XM_059422), a gene which inhibits thrombin, trypsin, and urokinase. binds heparin. promotes neurite extension. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINE2. The function of SERPINE2 has been established by previous studies. Protease nexin I is the most important physiologic regulator of alpha-thrombin in tissues. PN1 is highly expressed and developmentally regulated in the nervous system where it is concentrated at neuromuscular junctions and also central synapses in the hippocampus and striatum. Approximately 10% of identified proteins at

mammalian neuromuscular junctions are serine protease inhibitors, consistent with their central role in balancing serine protease activity to develop, maintain, and remodel synapses. By Southern blot hybridization of PN1 cDNA to somatic cell hybrid DNAs, Carter et al. (1995) mapped the PN1 gene, also known as PI7, to 2q33–q35. The regional localization was achieved by studying microcell hybrids that retained fragments of chromosome 2. The gene was located between the markers CRYGA (OMIM Ref. No. 123660) and MYL1 (OMIM Ref. No. 160780), both of which are located in the 2q33–q35 region. Further observations indicated that PN1 is close to MYL1 and farther removed from CRYGA. By hybrid cell methods, Carter et al. (1995) mapped the homologous gene to mouse chromosome 1 and sheep 2q, which are known to have regions of homology of synteny to human 2q. Carter et al. (1995) noted that a form of juvenile-onset amyotrophic lateral sclerosis maps to this same region of chromosome 2, making PN1 a candidate gene. The mammalian sex-determining pathway is controlled by the presence or absence of SRY (OMIM Ref. No. 480000) expression in the embryonic gonad. In order to identify additional sex-determining or gonadal differentiation genes, Grimmond

et al. (2000) screened for genes exhibiting sexually dimorphic patterns of expression in the mouse gonad at 12.5 and 13.5 days postcoitum, after overt gonad differentiation, by comparing complex cDNA probes derived from male and female gonadal tissue at these stages on microarrays constructed from a normalized urogenital ridge library. Using in situ hybridization analysis, they determined that mouse Pn1 and vanin-1 (OMIM Ref. No. 603570) exhibit male-specific expression prior to overt gonadal differentiation and are detected in the somatic portion of the developing gonad, suggesting to the authors a possible direct link to the testis-determining pathway for both genes. . Grimmond, S.; Van Hateren, N.; Siggers, P.; Arkell, R.; Larder, R.; Soares, M. B.; de Fatima Bonaldo, M.; Smith, L.; Tymowska-Lalanne, Z.; Wells, C.; Greenfield, A. : Sexually dimorphic expression of protease nexin-1 and vanin-1 in the developing mouse gonad prior to overt differentiation suggests a role in mammalian sexual development. Hum. Molec. Genet. 9: 1553-1560, 2000. PubMed ID : 10888606

[14236] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [14237] Carter, R. E.; Cerosaletti, K. M.; Burkin, D. J.; Fournier, R. E. K.; Jones, C.; Greenberg, B. D.; Citron, B. A.; Festoff, B. W. : The gene for the serpin thrombin inhibitor (P17), pro-tease nexin 1, is located on human chromosome 2q33–q35 and on syntenic regions in the mouse and sheep genomes. *Genomics* 27: 196–199, 1995. ; and
- [14238] Grimmond, S.; Van Hateren, N.; Siggers, P.; Arkell, R.; Larder, R.; Soares, M. B.; de Fatima Bonaldo, M.; Smith, L.; Tymowska-Lalanne, Z.; Wells, C.; Greenfield, A. : Sexually dimorphic ex.
- [14239] Further studies establishing the function and utilities of SERPINE2 are found in John Hopkins OMIM database record ID 177010, and in cited publications numbered 2752–2753, 1 and 1160–1161 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749) is another VGAM232 host target gene. SLC20A2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC20A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

SLC20A2 BINDING SITE, designated SEQ ID:13603, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14240] Another function of VGAM232 is therefore inhibition of Solute Carrier Family 20 (phosphate transporter), Member 2 (SLC20A2, Accession NM_006749), a gene which is a sodium–phosphate symporter. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC20A2. The function of SLC20A2 has been established by previous studies. The host range of retroviruses is determined primarily by the presence of specific receptors on target cells which are recognized by the retroviral envelope glycoprotein. Somatic cell hybrids have been used to determine the chromosomal location of several retroviral receptors in mice prior to their molecular cloning. By use of human–Chinese hamster somatic cell hybrids and a retroviral vector, Garcia et al. (1991) mapped the receptor for the amphotropic murine leukemia virus to the pericentromeric region of human chromosome 8. Kaelbling et al. (1991) described a receptor for the gibbon ape leukemia retrovirus. In an effort to isolate related human genes to determine if these function as receptors for any other

retroviruses, van Zeijl et al. (1993, 1994) screened a human cDNA library at low stringency using GLVR1 (OMIM Ref. No. 137570) as a probe. A single GLVR1-related cDNA (designated GLVR2) was isolated and found to have 62% identity to GLVR1 and its amino acid sequence. Using a somatic cell hybrid panel, GLVR2 was found to map to human chromosome 8, a location distinct from that for GLVR1, which maps to human chromosome 2. The location of GLVR2 on chromosome 8 highlighted the possibility that the locus may encode a receptor for the murine amphotropic virus because a receptor gene (MLVAR) for this virus was mapped to chromosome 8 by Garcia et al. (1991). Expression of GLVR2 in CHO-K1 cells, which are resistant to infection by amphotropic virus because of the absence of a receptor, rendered the cells sensitive to infection by the virus. Thus, GLVR2 is a receptor for amphotropic virus. It was pointed out by van Zeijl et al. (1994) that expression of the GLVR2 protein might be a requirement for infection of human cells by amphotropic retroviral vectors for purposes of gene therapy.

[14241] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14242] van Zeijl, M.; Johann, S. V.; Closs, E.; Cunningham, J.; Eddy, R.; Shows, T. B.; O'Hara, B. : A human amphotropic retrovirus receptor is a second member of the gibbon ape leukemia virus receptor family. *Proc. Nat. Acad. Sci.* 91: 1168–1172, 1994. ; and

[14243] Garcia, J. V.; Jones, C.; Miller, A. D. : Localization of the amphotropic murine leukemia virus receptor gene to the pericentromeric region of human chromosome 8. *J. Virol.* 65: 6316–6319.

[14244] Further studies establishing the function and utilities of SLC20A2 are found in John Hopkins OMIM database record ID 158378, and in cited publications numbered 380 and 4026–3802 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459) is another VGAM232 host target gene. SLC30A3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC30A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC30A3 BINDING SITE, designated SEQ ID:9527, to the nucleotide sequence of

VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14245] Another function of VGAM232 is therefore inhibition of Solute Carrier Family 30 (zinc transporter), Member 3 (SLC30A3, Accession NM_003459). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC30A3. Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184) is another VGAM232 host target gene. SPON1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPON1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPON1 BINDING SITE, designated SEQ ID:31301, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14246] Another function of VGAM232 is therefore inhibition of Spondin 1, (f-spondin) Extracellular Matrix Protein (SPON1, Accession XM_031184). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPON1.

Vascular Endothelial Growth Factor (VEGF, Accession NM_003376) is another VGAM232 host target gene. VEGF BINDING SITE1 and VEGF BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by VEGF, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VEGF BINDING SITE1 and VEGF BINDING SITE2, designated SEQ ID:9408 and SEQ ID:9409 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14247] Another function of VGAM232 is therefore inhibition of Vascular Endothelial Growth Factor (VEGF, Accession NM_003376), a gene which induces endothelial cell proliferation and vascular permeability. Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VEGF. The function of VEGF has been established by previous studies. To explore the possibility that VEGF and angiopoietins (see OMIM Ref. No. ANG2, 601922) collaborate during tumor angiogenesis, Holash et al. (1999) analyzed several different murine and human tumor models. Holash et al.

(1999) noted that angiopoietin-1 (ANG1; 601667) was antiapoptotic for cultured endothelial cells and expression of its antagonist angiopoietin-2 was induced in the endothelium of co-opted tumor vessels before their regression. In contrast, marked induction of VEGF expression occurred much later in tumor progression, in the hypoxic periphery of tumor cells surrounding the few remaining internal vessels, as well as adjacent to the robust plexus of vessels at the tumor margin. Expression of Ang2 in the few surviving internal vessels and in the angiogenic vessels at the tumor margin suggested that the destabilizing action of angiopoietin-2 facilitates the angiogenic action of VEGF at the tumor rim. Holash et al. (1999) implanted rat RBA mammary adenocarcinoma cells into rat brains. Tumor cells rapidly associated with and migrated along cerebral blood vessels. There was minimal upregulation of VEGF. Holash et al. (1999) suggested that a subset of tumors rapidly co-opts existing host vessels to form an initially well vascularized tumor mass. Perhaps as part of a host defense mechanism there is widespread regression of these initially co-opted vessels, leading to a secondarily avascular tumor and a massive tumor cell loss. However, the remaining tumor is ultimately rescued by robust an-

giogenesis at the tumor margin. Animal model experiments lend further support to the function of VEGF. De Fraipont et al. (2000) measured the cytosolic concentrations of 3 proteins involved in angiogenesis, namely, platelet-derived endothelial cell growth factor (PDEC GF; 131222), VEGFA, and thrombospondin-1 (THBS1; 188060) in a series of 43 human sporadic adrenocortical tumors. The tumors were classified as adenomas, transitional tumors, or carcinomas. PDEC GF/thymidine phosphorylase levels were not significantly different among these 3 groups. One hundred percent of the adenomas and 73% of the transitional tumors showed VEGFA concentrations under the threshold value of 107 ng/g protein, whereas 75% of the carcinomas had VEGFA concentrations above this threshold value. Similarly, 89% of the adenomas showed THBS1 concentrations above the threshold value of 57 microg/g protein, whereas only 25% of the carcinomas and 33% of the transitional tumor samples did so. IGF2 (OMIM Ref. No. 147470) overexpression, a common genetic alteration of adrenocortical carcinomas, was significantly correlated with higher VEGFA and lower THBS1 concentrations. The authors concluded that a decrease in THBS1 expression is an event that precedes an increase in VEGFA

expression during adrenocortical tumor progression. The population of premalignant tumors with low THBS1 and normal VEGFA levels could represent a selective target for antiangiogenic therapies.

[14248] It is appreciated that the abovementioned animal model for VEGF is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14249] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14250] Holash, J.; Maisonpierre, P. C.; Compton, D.; Boland, P.; Alexander, C. R.; Zagzag, D.; Yancopoulos, G. D.; Wiegand, S. J. : Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF. Science 284: 1994–1998, 1999. ; and

[14251] de Fraipont, F.; El Atifi, M.; Gicquel, C.; Bertagna, X.; Chambaz, E. M.; Feige, J. J. : Expression of the angiogenesis markers vascular endothelial growth factor-A, thrombospondin-1, and.

[14252] Further studies establishing the function and utilities of VEGF are found in John Hopkins OMIM database record ID 192240, and in cited publications numbered 3273,

11896, 10431–10432, 10516–10435, 11162–10442, 10595, 11761–1045 and 10479–9662 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Accession NM_014405) is another VGAM232 host target gene. CACNG4 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CACNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNG4 BINDING SITE, designated SEQ ID:15745, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14253] Another function of VGAM232 is therefore inhibition of Calcium Channel, Voltage-dependent, Gamma Subunit 4 (CACNG4, Accession NM_014405). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNG4. Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294) is another VGAM232 host target gene. CAMKK1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by CAMKK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK1 BINDING SITE, designated SEQ ID:26069, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14254] Another function of VGAM232 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 1, Alpha (CAMKK1, Accession NM_032294). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK1. CAMP-GEFII (Accession NM_007023) is another VGAM232 host target gene. CAMP-GEFII BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAMP-GEFII, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMP-GEFII BINDING SITE, designated SEQ ID:13882, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14255] Another function of VGAM232 is therefore inhibition of

CAMP-GEFII (Accession NM_007023). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMP-GEFII. Claudin 7 (CLDN7, Accession NM_001307) is another VGAM232 host target gene. CLDN7 BINDING SITE1 and CLDN7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CLDN7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLDN7 BINDING SITE1 and CLDN7 BINDING SITE2, designated SEQ ID:6989 and SEQ ID:45384 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14256] Another function of VGAM232 is therefore inhibition of Claudin 7 (CLDN7, Accession NM_001307). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLDN7. Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295) is another VGAM232 host target gene. EPB41L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by EPB41L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EPB41L1 BINDING SITE, designated SEQ ID:34941, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14257] Another function of VGAM232 is therefore inhibition of Erythrocyte Membrane Protein Band 4.1-like 1 (EPB41L1, Accession XM_047295). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EPB41L1. FLJ20886 (Accession XM_170820) is another VGAM232 host target gene. FLJ20886 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20886, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20886 BINDING SITE, designated SEQ ID:45595, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14258] Another function of VGAM232 is therefore inhibition of

FLJ20886 (Accession XM_170820). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20886. FLJ23024 (Accession NM_024936) is another VGAM232 host target gene. FLJ23024 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23024, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23024 BINDING SITE, designated SEQ ID:24473, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14259] Another function of VGAM232 is therefore inhibition of FLJ23024 (Accession NM_024936). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23024. FLJ31709 (Accession NM_144636) is another VGAM232 host target gene. FLJ31709 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ31709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ31709 BINDING SITE, designated SEQ ID:29457, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14260] Another function of VGAM232 is therefore inhibition of FLJ31709 (Accession NM_144636). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31709. GPCR150 (Accession NM_014373) is another VGAM232 host target gene. GPCR150 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPCR150, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPCR150 BINDING SITE, designated SEQ ID:15708, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14261] Another function of VGAM232 is therefore inhibition of GPCR150 (Accession NM_014373). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPCR150. HELO1 (Accession NM_021814) is another VGAM232 host

target gene. HELO1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by HELO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HELO1 BINDING SITE, designated SEQ ID:22384, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14262] Another function of VGAM232 is therefore inhibition of HELO1 (Accession NM_021814). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HELO1. IDI2 (Accession NM_033261) is another VGAM232 host target gene. IDI2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by IDI2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IDI2 BINDING SITE, designated SEQ ID:27092, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14263] Another function of VGAM232 is therefore inhibition of IDI2 (Accession NM_033261). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IDI2. KIAA0515 (Accession XM_033380) is another VGAM232 host target gene. KIAA0515 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0515, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0515 BINDING SITE, designated SEQ ID:31926, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14264] Another function of VGAM232 is therefore inhibition of KIAA0515 (Accession XM_033380). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0515. KIAA0561 (Accession XM_038150) is another VGAM232 host target gene. KIAA0561 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0561, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0561 BINDING SITE, designated SEQ ID:32765, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14265] Another function of VGAM232 is therefore inhibition of KIAA0561 (Accession XM_038150). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0561. KIAA1052 (Accession NM_014956) is another VGAM232 host target gene. KIAA1052 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1052, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1052 BINDING SITE, designated SEQ ID:17314, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14266] Another function of VGAM232 is therefore inhibition of KIAA1052 (Accession NM_014956). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1052. KIAA1509 (Accession XM_029353) is another VGAM232 host target gene. KIAA1509 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1509, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1509 BINDING SITE, designated SEQ ID:30874, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14267] Another function of VGAM232 is therefore inhibition of KIAA1509 (Accession XM_029353). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1509. KIAA1855 (Accession XM_166453) is another VGAM232 host target gene. KIAA1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1855 BINDING SITE, designated SEQ ID:44360, to the nucleotide sequence of VGAM232 RNA, herein designated

VGAM RNA, also designated SEQ ID:2943.

[14268] Another function of VGAM232 is therefore inhibition of KIAA1855 (Accession XM_166453). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1855. LIM and SH3 Protein 1 (LASP1, Accession NM_006148) is another VGAM232 host target gene. LASP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LASP1 BINDING SITE, designated SEQ ID:12800, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14269] Another function of VGAM232 is therefore inhibition of LIM and SH3 Protein 1 (LASP1, Accession NM_006148). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LASP1. MGC13057 (Accession NM_032321) is another VGAM232 host target gene. MGC13057 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

MGC13057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13057 BINDING SITE, designated SEQ ID:26126, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14270] Another function of VGAM232 is therefore inhibition of MGC13057 (Accession NM_032321). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13057. Netrin 4 (NTN4, Accession XM_031896) is another VGAM232 host target gene. NTN4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NTN4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NTN4 BINDING SITE, designated SEQ ID:31514, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14271] Another function of VGAM232 is therefore inhibition of Netrin 4 (NTN4, Accession XM_031896). Accordingly, util-

ities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NTN4. PPI5PIV (Accession NM_019892) is another VGAM232 host target gene. PPI5PIV BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPI5PIV, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPI5PIV BINDING SITE, designated SEQ ID:21276, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14272] Another function of VGAM232 is therefore inhibition of PPI5PIV (Accession NM_019892). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPI5PIV. SKIP (Accession NM_016532) is another VGAM232 host target gene. SKIP BINDING SITE1 and SKIP BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SKIP, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SKIP BINDING

SITE1 and SKIP BINDING SITE2, designated SEQ ID:18598 and SEQ ID:28261 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14273] Another function of VGAM232 is therefore inhibition of SKIP (Accession NM_016532). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SKIP. ZNF340 (Accession XM_097701) is another VGAM232 host target gene. ZNF340 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ZNF340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF340 BINDING SITE, designated SEQ ID:41033, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14274] Another function of VGAM232 is therefore inhibition of ZNF340 (Accession XM_097701). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF340. LOC113763 (Accession NM_138434) is another VGAM232

host target gene. LOC113763 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC113763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC113763 BINDING SITE, designated SEQ ID:28802, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14275] Another function of VGAM232 is therefore inhibition of LOC113763 (Accession NM_138434). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC113763. LOC145482 (Accession XM_085154) is another VGAM232 host target gene. LOC145482 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145482 BINDING SITE, designated SEQ ID:37877, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14276] Another function of VGAM232 is therefore inhibition of LOC145482 (Accession XM_085154). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145482. LOC145694 (Accession XM_096838) is another VGAM232 host target gene. LOC145694 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145694, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145694 BINDING SITE, designated SEQ ID:40557, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14277] Another function of VGAM232 is therefore inhibition of LOC145694 (Accession XM_096838). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145694. LOC149171 (Accession XM_086450) is another VGAM232 host target gene. LOC149171 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149171, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149171 BINDING SITE, designated SEQ ID:38667, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14278] Another function of VGAM232 is therefore inhibition of LOC149171 (Accession XM_086450). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149171. LOC149706 (Accession XM_097718) is another VGAM232 host target gene. LOC149706 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149706, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149706 BINDING SITE, designated SEQ ID:41058, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14279] Another function of VGAM232 is therefore inhibition of LOC149706 (Accession XM_097718). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC149706. LOC164382 (Accession XM_104390) is another VGAM232 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42164, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14280] Another function of VGAM232 is therefore inhibition of LOC164382 (Accession XM_104390). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC166042 (Accession XM_093623) is another VGAM232 host target gene. LOC166042 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC166042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC166042 BINDING SITE, designated SEQ ID:40200, to the nucleotide sequence of VGAM232 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2943.

[14281] Another function of VGAM232 is therefore inhibition of LOC166042 (Accession XM_093623). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC166042. LOC204161 (Accession XM_118480) is another VGAM232 host target gene. LOC204161 BINDING SITE1 and LOC204161 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC204161, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204161 BINDING SITE1 and LOC204161 BINDING SITE2, designated SEQ ID:43580 and SEQ ID:43581 respectively, to the nucleotide sequence of VGAM232 RNA, herein designated VGAM RNA, also designated SEQ ID:2943.

[14282] Another function of VGAM232 is therefore inhibition of LOC204161 (Accession XM_118480). Accordingly, utilities of VGAM232 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204161. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 233 (VGAM233) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14283] VGAM233 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM233 was detected is described hereinabove with reference to Figs. 1–8.

[14284] VGAM233 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14285] VGAM233 gene encodes a VGAM233 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM233

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM233 precursor RNA is designated SEQ ID:219, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:219 is located at position 55213 relative to the genome of Calitrichine Herpesvirus 3.

[14286] VGAM233 precursor RNA folds onto itself, forming VGAM233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14287] An enzyme complex designated DICER COMPLEX, `dices` the VGAM233 folded precursor RNA into VGAM233 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 60%) nucleotide sequence of VGAM233 RNA is designated SEQ ID:2944, and is provided hereinbelow with reference to the sequence listing part.

[14288] VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM233 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[14289] VGAM233 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM233 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM233 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14290] The complementary binding of VGAM233 RNA, herein designated VGAM RNA, to host target binding sites on VGAM233 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM233 host target RNA into VGAM233 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14291] It is appreciated that VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM233 host target genes. The mRNA of each one of this plurality of VGAM233 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM233 RNA, herein designated VGAM RNA, and which when bound by VGAM233 RNA causes inhibition of translation of respective one or more VGAM233 host target proteins.

[14292] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM233 gene, herein designated VGAM GENE, on one or more VGAM233 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14293] It is yet further appreciated that a function of VGAM233 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM233 correlate with, and may be deduced from, the identity of the host target genes which VGAM233 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14294] Nucleotide sequences of the VGAM233 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM233 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM233 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM233 are further described hereinbelow with reference to Table 1.

[14295] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM233 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM233 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[14296] As mentioned hereinabove with reference to Fig. 1, a function of VGAM233 gene, herein designated VGAM is inhibition of expression of VGAM233 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM233 correlate with, and may be deduced from, the identity of the target genes which VGAM233 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14297] Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718) is a VGAM233 host target gene. BMP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BMP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP6 BINDING SITE, designated SEQ ID:7454, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14298] A function of VGAM233 is therefore inhibition of Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718), a gene which induces cartilage and bone formation. Accordingly, utilities of VGAM233 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with BMP6. The function of BMP6 has been established by previous studies. See BMP5 (OMIM Ref. No. 112265). Hahn et al. (1992) mapped both BMP5 and BMP6 to human chromosome 6 by study of human/rodent somatic cell hybrid lines with cDNA probes. Olavesen et al. (1997) reported fine mapping of 39 ESTs on 6p25–p23. Most of the ESTs (31 of 39) were positioned in the 6p24–p23 interval; of these, 8 were located within a single PAC clone. BMP6 was 1 of the 8 loci on the PAC, between TFAP2 (OMIM Ref. No. 107580) at the centromeric side and DSP (OMIM Ref. No. 125647) on the telomeric side. Rickard et al. (1998) presented evidence that the skeletal effects of estrogen on bone and cartilage may be mediated by increased production of BMP6 by osteoblasts. They investigated the effect of estrogen on BMP production in 2 estrogen-responsive, human immortalized cell lines that display the mature osteoblast phenotype.

[14299] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14300] Hahn, G. V.; Cohen, R. B.; Wozney, J. M.; Levitz, C. L.; Shore, E. M.; Zasloff, M. A.; Kaplan, F. S. : A bone morpho-

genetic protein subfamily: chromosomal localization of human genes for BMP5, BMP6, and BMP7. Genomics 14: 759–762, 1992. ; and

[14301] Rickard, D. J.; Hofbauer, L. C.; Bonde, S. K.; Gori, F.; Spelsberg, T. C.; Riggs, B. L. : Bone morphogenetic protein–6 production in human osteoblastic cell lines: selective regulation b.

[14302] Further studies establishing the function and utilities of BMP6 are found in John Hopkins OMIM database record ID 112266, and in cited publications numbered 2714–191 and 4585 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calcium Channel, Voltage–dependent, Beta 1 Subunit (CACNB1, Accession NM_000723) is another VGAM233 host target gene. CACNB1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CACNB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNB1 BINDING SITE, designated SEQ ID:6386, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14303] Another function of VGAM233 is therefore inhibition of Calcium Channel, Voltage-dependent, Beta 1 Subunit (CACNB1, Accession NM_000723), a gene which may not only play an important role in the transport/insertion of the alpha-1S subunit into the membrane. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNB1. The function of CACNB1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM114. Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is another VGAM233 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20735, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14304] Another function of VGAM233 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession

NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM_003633) is another VGAM233 host target gene. ENC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ENC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENC1 BINDING SITE, designated SEQ ID:9698, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14305] Another function of VGAM233 is therefore inhibition of Ectodermal-neural Cortex (with BTB-like domain) (ENC1, Accession NM_003633), a gene which is an actin-binding protein involved in the regulation of neuronal process formation and in differentiation of neural crest cells. Accord-

ingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENC1. The function of ENC1 has been established by previous studies. DNA damage and/or hyperproliferative signals activate wildtype p53 tumor suppressor protein (TP53; 191170), inducing cell cycle arrest or apoptosis. Mutations that inactivate p53 occur in 50% of all tumors. Polyak et al. (1997) used serial analysis of gene expression (SAGE) to evaluate cellular mRNA levels in a colorectal cancer cell line transfected with p53. Of 7,202 transcripts identified, only 14 were expressed at levels more than 10-fold higher in p53-expressing cells than in control cells. Polyak et al. (1997) termed these genes 'p53-induced genes,' or PIGs, several of which were predicted to encode redox-controlling proteins. They noted that reactive oxygen species (ROS) are potent inducers of apoptosis. Flow cytometric analysis showed that p53 expression induces ROS production, which increases as apoptosis progresses under some conditions. The authors stated that the PIG10 gene, also called ENC1, encodes an actin-binding protein. By screening fetal and adult hippocampus cDNA libraries using a brain development-related cDNA as the probe, Kim et al. (1998) obtained cD-

NAs encoding ENC1, which they called NRPB (nuclear-restricted protein/brain). Human and mouse ENC1 share 99% amino acid identity. The deduced 589-amino acid ENC1 protein has a 114-amino acid BTB/POZ-like domain in the alpha-helical N terminus and a beta sheet bearing a 50-amino acid 'kelch' motif repeated 6 times in the C terminus. The kelch motif invariably contains 2 adjacent glycine residues and shares homology with several actin-associated proteins, including the *Drosophila* kelch protein. Northern blot analysis detected abundant expression of a 5.5-kb ENC1 transcript in fetal brain, with moderate expression in fetal heart, lung, and kidney. In adult tissues, high levels of ENC1 were detected in brain, particularly in amygdala and hippocampus, and lower levels were detected in pancreas. In 12 day- but not 10 day-postcoitus mouse embryos, expression of Enc1 was 50-fold higher in brain than in other tissues. Immunoprecipitation and Western blot analysis showed that ENC1 is expressed as a 67-kD protein in nuclear pellets and as 67- and 57-kD proteins in total cell lysates from primary neurons. Western blot analysis, immunofluorescence, and confocal microscopy demonstrated that Enc1 is expressed in the nuclear matrix of rat hippocampal neu-

rons but not at all in astrocytes. By searching an EST database for homologs of mouse *Enc1*, Hernandez et al. (1998) identified human *ENC1*. Northern blot analysis detected abundant expression of an approximately 4.5-kb *ENC1* transcript in brain, with lower expression in pancreas and no expression in other tissues. Within the central nervous system, expression was highest in cerebral cortex, frontal and temporal lobes, putamen, and spinal cord; lower expression was found in medulla and cerebellum, and very low levels of expression were found in the occipital pole. Low levels of *ENC1* were also detected in a variety of neural tumor cell lines. *ENC1* expression increased dramatically in a neuroblastoma cell line undergoing retinoic acid-induced differentiation. By differential display, Zhao et al. (2000) identified rat *Enc1* as a transcript associated with differentiation of rat preadipocytes in primary culture. Using the fragment identified by differential display as probe, they cloned full-length *Enc1* cDNA from a mouse brain cDNA library. By Northern blot analysis of rat tissues, Zhao et al. (2000) found high expression in brain, low expression in testis, and no expression in other tissues tested. They also found high expression of *Enc1* in the stroma-vascular fraction of adipose

tissue but very little in mature adipocyte fraction. Transient transfection in a 3T3 fibroblastic preadipocyte cell line resulted in subcellular colocalization with F-actin (OMIM Ref. No. 102560). Kim et al. (1998) showed that expression of ENC1 induced neuronal process formation, whereas antisense treatment inhibited neurite development. Immunoblot analysis showed that ENC1 can be phosphorylated and binds to the functionally active hypophosphorylated form of the nuclear matrix protein RB1 (OMIM Ref. No. 180200) during neuronal differentiation. Using primary cell culture of rat stroma-vascular cells, Zhao et al. (2000) found that transient early expression of Enc1 preceded the conversion of the fibroblastic preadipocytes to mature adipose. Enc1 expression also preceded expression of adipocyte-specific markers, including transcription factors known to activate adipocyte genes. Antisense transfection blocked differentiation to the mature adipocyte morphology.

[14306] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14307] Zhao, L.; Gregoire, F.; Sul, H. S. : Transient induction of ENC-1, a kelch-related actin-binding protein, is required

for adipocyte differentiation. J. Biol. Chem. 275:

16845–16850, 2000. ; and

[14308] Hernandez, M.-C.; Andres-Barquin, P. J.; Israel, M. A. : Assignment of the ectodermal-neural cortex 1 gene (Enc1) to mouse chromosome band 13D1 by fluorescence in situ hybridization. Cy.

[14309] Further studies establishing the function and utilities of ENC1 are found in John Hopkins OMIM database record ID 605173, and in cited publications numbered 2332–2335, 233 and 4795 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_012300) is another VGAM233 host target gene. FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FBXW1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXW1B BINDING SITE1 through FBXW1B BINDING SITE3, designated SEQ ID:14662, SEQ ID:27364 and SEQ ID:27374 respectively, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ

ID:2944.

[14310] Another function of VGAM233 is therefore inhibition of F-box and WD-40 Domain Protein 1B (FBXW1B, Accession NM_012300), a gene which somehow is involved in the process of neuronal cell differentiation or brain development. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXW1B. The function of FBXW1B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM25.Protocadherin Gamma Subfamily A, 11

(PCDHGA11, Accession NM_018914) is another VGAM233 host target gene. PCDHGA11 BINDING SITE1 through PCDHGA11 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PCDHGA11, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCDHGA11 BINDING SITE1 through PCDHGA11 BINDING SITE3, designated SEQ ID:20983, SEQ ID:25788 and SEQ ID:25789 respectively, to the nucleotide sequence of VGAM233 RNA, herein designated

VGAM RNA, also designated SEQ ID:2944.

[14311] Another function of VGAM233 is therefore inhibition of Protocadherin Gamma Subfamily A, 11 (PCDHGA11, Accession NM_018914). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCDHGA11. Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112) is another VGAM233 host target gene. TRPS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPS1 BINDING SITE, designated SEQ ID:15349, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14312] Another function of VGAM233 is therefore inhibition of Trichorhinophalangeal Syndrome I (TRPS1, Accession NM_014112), a gene which may function as a transcriptional activator protein. Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPS1. The function of TRPS1 and its association with various diseases

and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172.A Kinase (PRKA) Anchor Protein (yotiao) 9 (AKAP9, Accession NM_005751) is another VGAM233 host target gene. AKAP9 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by AKAP9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AKAP9 BINDING SITE, designated SEQ ID:12313, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14313] Another function of VGAM233 is therefore inhibition of A Kinase (PRKA) Anchor Protein (yotiao) 9 (AKAP9, Accession NM_005751). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP9. Rho GDP Dissociation Inhibitor (GDI) Gamma (ARHGDIG, Accession NM_001176) is another VGAM233 host target gene. ARHGDIG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ARHGDIG, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGDIG BINDING SITE, designated SEQ ID:6851, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14314] Another function of VGAM233 is therefore inhibition of Rho GDP Dissociation Inhibitor (GDI) Gamma (ARHGDIG, Accession NM_001176). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGDIG.

FLJ00001 (Accession XM_088525) is another VGAM233 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ00001 BINDING SITE, designated SEQ ID:39776, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14315] Another function of VGAM233 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of

VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ13842 (Accession NM_024645) is another VGAM233 host target gene. FLJ13842 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13842 BINDING SITE, designated SEQ ID:23928, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14316] Another function of VGAM233 is therefore inhibition of FLJ13842 (Accession NM_024645). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13842. Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM_004485) is another VGAM233 host target gene. GNG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GNG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of GNG4 BINDING SITE, designated SEQ ID:10808, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14317] Another function of VGAM233 is therefore inhibition of Guanine Nucleotide Binding Protein (G protein), Gamma 4 (GNG4, Accession NM_004485). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GNG4. Potassium Voltage-gated Channel, Delayed-rectifier, Sub-family S, Member 1 (KCNS1, Accession NM_002251) is another VGAM233 host target gene. KCNS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KCNS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNS1 BINDING SITE, designated SEQ ID:8042, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14318] Another function of VGAM233 is therefore inhibition of Potassium Voltage-gated Channel, Delayed-rectifier, Sub-family S, Member 1 (KCNS1, Accession NM_002251). Ac-

cordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNS1. KIAA0513 (Accession NM_014732) is another VGAM233 host target gene. KIAA0513 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0513, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0513 BINDING SITE, designated SEQ ID:16352, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14319] Another function of VGAM233 is therefore inhibition of KIAA0513 (Accession NM_014732). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0513. KIAA0555 (Accession NM_014790) is another VGAM233 host target gene. KIAA0555 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0555, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA0555 BINDING SITE, designated SEQ ID:16683, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14320] Another function of VGAM233 is therefore inhibition of KIAA0555 (Accession NM_014790). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0555. KIAA1497 (Accession XM_041431) is another VGAM233 host target gene. KIAA1497 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1497, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1497 BINDING SITE, designated SEQ ID:33526, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14321] Another function of VGAM233 is therefore inhibition of KIAA1497 (Accession XM_041431). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1497. Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379) is another VGAM233

host target gene. MAN1C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAN1C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAN1C1 BINDING SITE, designated SEQ ID:21644, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14322] Another function of VGAM233 is therefore inhibition of Mannosidase, Alpha, Class 1C, Member 1 (MAN1C1, Accession NM_020379). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAN1C1. LOC124402 (Accession NM_145253) is another VGAM233 host target gene. LOC124402 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124402, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124402 BINDING SITE, designated SEQ ID:29766, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA,

also designated SEQ ID:2944.

[14323] Another function of VGAM233 is therefore inhibition of LOC124402 (Accession NM_145253). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124402. LOC142955 (Accession XM_084389) is another VGAM233 host target gene. LOC142955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC142955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC142955 BINDING SITE, designated SEQ ID:37573, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14324] Another function of VGAM233 is therefore inhibition of LOC142955 (Accession XM_084389). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC142955. LOC147054 (Accession XM_097172) is another VGAM233 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40790, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14325] Another function of VGAM233 is therefore inhibition of LOC147054 (Accession XM_097172). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147054. LOC150538 (Accession XM_086945) is another VGAM233 host target gene. LOC150538 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150538 BINDING SITE, designated SEQ ID:38991, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14326] Another function of VGAM233 is therefore inhibition of LOC150538 (Accession XM_086945). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC150538. LOC153454 (Accession XM_087672) is another VGAM233 host target gene. LOC153454 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC153454, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153454 BINDING SITE, designated SEQ ID:39374, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14327] Another function of VGAM233 is therefore inhibition of LOC153454 (Accession XM_087672). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153454. LOC196411 (Accession XM_113714) is another VGAM233 host target gene. LOC196411 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC196411, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196411 BINDING SITE, designated SEQ ID:42363, to

the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14328] Another function of VGAM233 is therefore inhibition of LOC196411 (Accession XM_113714). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196411. LOC200317 (Accession XM_114208) is another VGAM233 host target gene. LOC200317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200317 BINDING SITE, designated SEQ ID:42802, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14329] Another function of VGAM233 is therefore inhibition of LOC200317 (Accession XM_114208). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200317. LOC200609 (Accession XM_117256) is another VGAM233 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43327, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14330] Another function of VGAM233 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC203595 (Accession XM_119962) is another VGAM233 host target gene. LOC203595 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203595, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203595 BINDING SITE, designated SEQ ID:43605, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14331] Another function of VGAM233 is therefore inhibition of LOC203595 (Accession XM_119962). Accordingly, utilities

of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203595. LOC254196 (Accession XM_173220) is another VGAM233 host target gene. LOC254196 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254196 BINDING SITE, designated SEQ ID:46476, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14332] Another function of VGAM233 is therefore inhibition of LOC254196 (Accession XM_173220). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254196. LOC255040 (Accession XM_172837) is another VGAM233 host target gene. LOC255040 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255040, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC255040 BINDING SITE, designated SEQ ID:46108, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14333] Another function of VGAM233 is therefore inhibition of LOC255040 (Accession XM_172837). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255040. LOC255041 (Accession XM_172838) is another VGAM233 host target gene. LOC255041 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255041, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255041 BINDING SITE, designated SEQ ID:46111, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14334] Another function of VGAM233 is therefore inhibition of LOC255041 (Accession XM_172838). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255041. LOC91907 (Accession XM_041430) is another VGAM233 host target gene. LOC91907 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91907, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91907 BINDING SITE, designated SEQ ID:33520, to the nucleotide sequence of VGAM233 RNA, herein designated VGAM RNA, also designated SEQ ID:2944.

[14335] Another function of VGAM233 is therefore inhibition of LOC91907 (Accession XM_041430). Accordingly, utilities of VGAM233 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91907. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 234 (VGAM234) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14336] VGAM234 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM234 was detected is described hereinabove with reference to Figs. 1-8.

[14337] VGAM234 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14338] VGAM234 gene encodes a VGAM234 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM234 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM234 precursor RNA is designated SEQ ID:220, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:220 is located at position 25253 relative to the genome of Callitrichine Herpesvirus 3.

[14339] VGAM234 precursor RNA folds onto itself, forming VGAM234 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[14340] An enzyme complex designated DICER COMPLEX, `dices` the VGAM234 folded precursor RNA into VGAM234 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM234 RNA is designated SEQ ID:2945, and is provided hereinbelow with reference to the sequence listing part.

[14341] VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM234 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14342] VGAM234 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM234 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM234 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM234 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14343] The complementary binding of VGAM234 RNA, herein designated VGAM RNA, to host target binding sites on VGAM234 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM234 host target RNA into VGAM234 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14344] It is appreciated that VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM234 host target genes. The mRNA of each one of this plurality of VGAM234 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM234 RNA, herein designated VGAM RNA, and which when bound by VGAM234 RNA causes inhibition of translation of respective one or more VGAM234 host target proteins.

[14345] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM234 gene, herein designated VGAM GENE, on one or more VGAM234 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14346] It is yet further appreciated that a function of VGAM234 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM234 correlate with, and may be deduced from, the identity of the host target genes which VGAM234 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14347] Nucleotide sequences of the VGAM234 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM234 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM234 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM234 are further described hereinbelow with reference to Table 1.

[14348] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM234 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM234 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14349] As mentioned hereinabove with reference to Fig. 1, a function of VGAM234 gene, herein designated VGAM is inhibition of expression of VGAM234 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM234 correlate with, and may be deduced from, the identity of the target genes which VGAM234 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14350] Adenosine A1 Receptor (ADORA1, Accession NM_000674) is a VGAM234 host target gene. ADORA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADORA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ADORA1 BINDING SITE, designated SEQ ID:6329, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14351] A function of VGAM234 is therefore inhibition of Adenosine A1 Receptor (ADORA1, Accession NM_000674), a gene which the activity of this receptor is mediated by G proteins which inhibit adenylyl cyclase. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADORA1. The function of ADORA1 has been established by previous studies. Diverse physiologic effects of adenosine were recognized as early as the 1920s (Drury and Szent-Gyorgyi, 1929; Berne, 1963). Once released, adenosine activates adenosine receptors, which in turn regulate a diverse set of physiologic functions including cardiac rate and contractility, smooth muscle tone, sedation, release of neurotransmitters, platelet function, lipolysis, renal function, and white blood cell function. Stiles (1992) reviewed the structure and function of adenosine receptors important in the mediation of these multiple effects. Also see adenosine A2 receptor (ADORA2A; 102776). Libert et al. (1991) obtained cDNA clones for 4

receptors of the G protein-coupled receptor family by selective amplification of cloning from thyroid cDNA and termed them RDC1 (VIPR1; 192321), RDC4 (HTR1D; 182133), RDC7, and RDC8 (ADORA2A). RDC7 and RDC8 were identified as A1 and A2 adenosine receptors, respectively. By in situ hybridization, Libert et al. (1991) assigned the RDC7 gene to 22q11.2-q13.1. However, using fluorescence in situ hybridization, Townsend-Nicholson et al. (1995) demonstrated that the ADORA1 gene is located on 1q32.1. Animal model experiments lend further support to the function of ADORA1. Sun et al. (2001) used homologous recombination to generate viable mice without gross behavioral or anatomic defects that were deficient in the 2-exon A1ar gene, which encodes a protein 87% identical to the human protein.

[14352] It is appreciated that the abovementioned animal model for ADORA1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14353] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14354] Stiles, G. L. : Adenosine receptors. J. Biol. Chem. 267:

6451–6454, 1992. ; and

[14355] Sun, D.; Samuelson, L. C.; Yang, T.; Huang, Y.; Paliege, A.; Saunders, T.; Briggs, J.; Schnermann, J. : Mediation of tubuloglomerular feedback by adenosine: evidence from mice lacking ad.

[14356] Further studies establishing the function and utilities of ADORA1 are found in John Hopkins OMIM database record ID 102775, and in cited publications numbered 12772–192 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CAMP Responsive Element Binding Protein–like 2 (CREBL2, Accession NM_001310) is another VGAM234 host target gene. CREBL2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CREBL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREBL2 BINDING SITE, designated SEQ ID:6997, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14357] Another function of VGAM234 is therefore inhibition of CAMP Responsive Element Binding Protein–like 2 (CREBL2,

Accession NM_001310). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREBL2. Early Growth Response 2 (Krox-20 homolog, Drosophila) (EGR2, Accession NM_000399) is another VGAM234 host target gene. EGR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EGR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGR2 BINDING SITE, designated SEQ ID:5972, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14358] Another function of VGAM234 is therefore inhibition of Early Growth Response 2 (Krox-20 homolog, Drosophila) (EGR2, Accession NM_000399), a gene which binds to two specific dna sites located in the promoter region of hox-1.4. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGR2. The function of EGR2 has been established by previous studies. Timmerman et al. (1999) screened 170 unrelated neuropathy patients and identified 2 with Dejerine-Sottas neuropathy (DSN;

145900) who had a heterozygous R359W mutation (129010.0004) in the alpha-helix domain of the first zinc finger of EGR2. Boerkoel et al. (2001) reported 2 additional DSN patients with the R359W mutation and suggested that it is the most common neuropathy-associated EGR2 mutation and consistently causes DSN. The expressivity ranged from that typical for DSN to a more rapidly progressive neuropathy that can cause death by age 6 years. Furthermore, in contrast to patients with typical DSN, patients with the EGR2 R359W mutation had more respiratory compromise and cranial nerve involvement. Animal model experiments lend further support to the function of EGR2. Congenital hypomyelinating neuropathy (CHN; 605253) is characterized clinically by early onset of hypotonia, areflexia, distal muscle weakness, and very slow nerve conduction velocities. Warner et al. (1997, 1998) noted that pathologic findings on sural nerve biopsies show hypomyelination of most or all fibers. Based on these findings, CHN is considered to be a result of congenital impairment in myelin formation. The disorder is inherited as an autosomal recessive. The EGR2 gene attracted the attention of Warner et al. (1997, 1998) as a potential candidate for CHN because of the expression

and knockout phenotype of its mouse homolog, Krox20. Krox20, a member of a multigene family of zinc finger proteins, is thought to function as an immediate early protein with basal expression in selected neuronal populations of the central and peripheral nervous systems. Krox20 knockout mice showed disrupted hindbrain segmentation and development and a block of Schwann cells at an early stage of differentiation as evidenced by the fact that the expression of early myelin genes, such as myelin-associated glycoprotein (OMIM Ref. No. 159460), are barely affected while the expression of the late myelin genes, myelin basic protein (OMIM Ref. No. 159430) and myelin protein zero (MPZ; 159440), are decreased or absent.

[14359] It is appreciated that the abovementioned animal model for EGR2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14360] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14361] Timmerman, V.; De Jonghe, P.; Ceuterick, C.; De Vriendt, E.; Lofgren, A.; Nelis, E.; Warner, L. E.; Lupski, J. R.; Martin,

J.-J.; Van Broeckhoven, C. : Novel missense mutation in the early growth response 2 gene associated with Dejerine-Sottas syndrome phenotype. *Neurology* 52: 1827-1832, 1999. ; and

[14362] Warner, L. E.; Mancias, P.; Butler, I. J.; McDonald, C. M.; Keppen, L.; Koob, K. G.; Lupski, J. R. : Mutations in the early growth response 2 (EGR2) gene are associated with hereditary.

[14363] Further studies establishing the function and utilities of EGR2 are found in John Hopkins OMIM database record ID 129010, and in cited publications numbered 1167 and 12036-12043 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fms-related Tyrosine Kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1, Accession NM_002019) is another VGAM234 host target gene. FLT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLT1 BINDING SITE, designated SEQ ID:7767, to the nucleotide sequence of VGAM234 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2945.

[14364] Another function of VGAM234 is therefore inhibition of Fms-related Tyrosine Kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor) (FLT1, Accession NM_002019). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLT1. GATA Binding Protein 3 (GATA3, Accession NM_002051) is another VGAM234 host target gene. GATA3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA3 BINDING SITE, designated SEQ ID:7808, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14365] Another function of VGAM234 is therefore inhibition of GATA Binding Protein 3 (GATA3, Accession NM_002051). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA3. LAPTM5 (Accession NM_006762) is another VGAM234 host target gene. LAPTM5 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LAPTM5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAPTM5 BINDING SITE, designated SEQ ID:13619, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14366] Another function of VGAM234 is therefore inhibition of LAPTM5 (Accession NM_006762). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAPTM5. Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession NM_002608) is another VGAM234 host target gene. PDGFB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDGFB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFB BINDING SITE, designated SEQ ID:8472, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14367] Another function of VGAM234 is therefore inhibition of Platelet-derived Growth Factor Beta Polypeptide (simian sarcoma viral (v-sis) Oncogene Homolog) (PDGFB, Accession NM_002608), a gene which plays an important role in stimulating adjacent cells to grow and thereby heal the wound. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFB. The function of PDGFB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173. Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043) is another VGAM234 host target gene. SLC6A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A6 BINDING SITE, designated SEQ ID:9008, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14368] Another function of VGAM234 is therefore inhibition of

Solute Carrier Family 6 (neurotransmitter transporter, taurine), Member 6 (SLC6A6, Accession NM_003043), a gene which transports taurine and other beta-amino acids like beta-alanine. Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A6. The function of SLC6A6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36. Tumor Necrosis Factor (ligand) Superfamily, Member 6 (TNFSF6, Accession NM_000639) is another VGAM234 host target gene. TNFSF6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF6 BINDING SITE, designated SEQ ID:6275, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14369] Another function of VGAM234 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 6 (TNFSF6, Accession NM_000639). Accordingly, utilities of

VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TNFSF6. Reserved (C8orf13, Accession XM_088377) is another VGAM234 host target gene. C8orf13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C8orf13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C8orf13 BINDING SITE, designated SEQ ID:39659, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14370] Another function of VGAM234 is therefore inhibition of Reserved (C8orf13, Accession XM_088377). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C8orf13. DKFZP434E2135 (Accession NM_030804) is another VGAM234 host target gene. DKFZP434E2135 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434E2135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of DKFZP434E2135 BINDING SITE, designated SEQ ID:25120, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14371] Another function of VGAM234 is therefore inhibition of DKFZP434E2135 (Accession NM_030804). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2135. DKFZp762L0311 (Accession NM_018719) is another VGAM234 host target gene. DKFZp762L0311 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp762L0311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp762L0311 BINDING SITE, designated SEQ ID:20800, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14372] Another function of VGAM234 is therefore inhibition of DKFZp762L0311 (Accession NM_018719). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZp762L0311. Endothelial Cell-specific Molecule 1 (ESM1, Accession NM_007036) is another VGAM234 host target gene. ESM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESM1 BINDING SITE, designated SEQ ID:13914, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14373] Another function of VGAM234 is therefore inhibition of Endothelial Cell-specific Molecule 1 (ESM1, Accession NM_007036). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESM1. FLJ13798 (Accession XM_102377) is another VGAM234 host target gene. FLJ13798 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13798, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13798 BINDING SITE, designated SEQ

ID:42112, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14374] Another function of VGAM234 is therefore inhibition of FLJ13798 (Accession XM_102377). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13798. FLJ20047 (Accession NM_017639) is another VGAM234 host target gene. FLJ20047 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ20047, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20047 BINDING SITE, designated SEQ ID:19145, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14375] Another function of VGAM234 is therefore inhibition of FLJ20047 (Accession NM_017639). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20047. G2 (Accession XM_039515) is another VGAM234 host target gene. G2 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of G2 BINDING SITE, designated SEQ ID:33114, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14376] Another function of VGAM234 is therefore inhibition of G2 (Accession XM_039515). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with G2.

KIAA0016 (Accession NM_014765) is another VGAM234 host target gene. KIAA0016 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0016, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0016 BINDING SITE, designated SEQ ID:16532, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14377] Another function of VGAM234 is therefore inhibition of KIAA0016 (Accession NM_014765). Accordingly, utilities

of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0016. KIAA1822 (Accession XM_041566) is another VGAM234 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33555, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14378] Another function of VGAM234 is therefore inhibition of KIAA1822 (Accession XM_041566). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. KOC1 (Accession XM_165847) is another VGAM234 host target gene. KOC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KOC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KOC1 BINDING SITE,

designated SEQ ID:43777, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14379] Another function of VGAM234 is therefore inhibition of KOC1 (Accession XM_165847). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KOC1. MEF-2 (Accession XM_034883) is another VGAM234 host target gene. MEF-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEF-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEF-2 BINDING SITE, designated SEQ ID:32182, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14380] Another function of VGAM234 is therefore inhibition of MEF-2 (Accession XM_034883). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEF-2. MGC20496 (Accession NM_052845) is another VGAM234 host target gene. MGC20496 BINDING SITE is HOST TAR-

GET binding site found in the 3' untranslated region of mRNA encoded by MGC20496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC20496 BINDING SITE, designated SEQ ID:27426, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14381] Another function of VGAM234 is therefore inhibition of MGC20496 (Accession NM_052845). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC20496. N4BP3 (Accession XM_038920) is another VGAM234 host target gene. N4BP3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by N4BP3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of N4BP3 BINDING SITE, designated SEQ ID:32942, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14382] Another function of VGAM234 is therefore inhibition of

N4BP3 (Accession XM_038920). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with N4BP3. PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975) is another VGAM234 host target gene. PTK6 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PTK6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTK6 BINDING SITE, designated SEQ ID:12602, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14383] Another function of VGAM234 is therefore inhibition of PTK6 Protein Tyrosine Kinase 6 (PTK6, Accession NM_005975). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTK6. LOC145622 (Accession XM_085186) is another VGAM234 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37903, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14384] Another function of VGAM234 is therefore inhibition of LOC145622 (Accession XM_085186). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC154092 (Accession XM_098466) is another VGAM234 host target gene. LOC154092 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154092 BINDING SITE, designated SEQ ID:41683, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14385] Another function of VGAM234 is therefore inhibition of LOC154092 (Accession XM_098466). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC154092. LOC170063 (Accession XM_104820) is another VGAM234 host target gene. LOC170063 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170063, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170063 BINDING SITE, designated SEQ ID:42185, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14386] Another function of VGAM234 is therefore inhibition of LOC170063 (Accession XM_104820). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170063. LOC205327 (Accession XM_115788) is another VGAM234 host target gene. LOC205327 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC205327, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205327 BINDING SITE, designated SEQ ID:43106, to the nucleotide sequence of VGAM234 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2945.

[14387] Another function of VGAM234 is therefore inhibition of LOC205327 (Accession XM_115788). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC205327. LOC221463 (Accession XM_166374) is another VGAM234 host target gene. LOC221463 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221463, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221463 BINDING SITE, designated SEQ ID:44206, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14388] Another function of VGAM234 is therefore inhibition of LOC221463 (Accession XM_166374). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221463. LOC221466 (Accession XM_168087) is another VGAM234 host target gene. LOC221466 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221466, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221466 BINDING SITE, designated SEQ ID:44997, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14389] Another function of VGAM234 is therefore inhibition of LOC221466 (Accession XM_168087). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221466. LOC51031 (Accession NM_016080) is another VGAM234 host target gene. LOC51031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51031 BINDING SITE, designated SEQ ID:18154, to the nucleotide sequence of VGAM234 RNA, herein designated VGAM RNA, also designated SEQ ID:2945.

[14390] Another function of VGAM234 is therefore inhibition of LOC51031 (Accession NM_016080). Accordingly, utilities of VGAM234 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC51031. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 235 (VGAM235) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14391] VGAM235 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM235 was detected is described hereinabove with reference to Figs. 1–8.

[14392] VGAM235 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14393] VGAM235 gene encodes a VGAM235 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM235 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM235 precursor RNA is designated SEQ

ID:221, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:221 is located at position 99717 relative to the genome of Calitrichine Herpesvirus 3.

[14394] VGAM235 precursor RNA folds onto itself, forming VGAM235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14395] An enzyme complex designated DICER COMPLEX, `dices` the VGAM235 folded precursor RNA into VGAM235 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM235 RNA is designated SEQ ID:2946, and is provided hereinbelow with reference to the sequence

listing part.

[14396] VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM235 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14397] VGAM235 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM235 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM235 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[14398] The complementary binding of VGAM235 RNA, herein designated VGAM RNA, to host target binding sites on VGAM235 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM235 host target RNA into VGAM235 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14399] It is appreciated that VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM235 host target genes. The mRNA of each one of this plurality of VGAM235 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM235 RNA, herein designated VGAM

RNA, and which when bound by VGAM235 RNA causes inhibition of translation of respective one or more VGAM235 host target proteins.

[14400] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM235 gene, herein designated VGAM GENE, on one or more VGAM235 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14401] It is yet further appreciated that a function of VGAM235 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM235 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM235 correlate with, and may be deduced from, the identity of the host target genes which VGAM235 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14402] Nucleotide sequences of the VGAM235 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM235 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM235 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM235 are further described hereinbelow with reference to Table 1.

[14403] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM235 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM235 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14404] As mentioned hereinabove with reference to Fig. 1, a function of VGAM235 gene, herein designated VGAM is

inhibition of expression of VGAM235 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM235 correlate with, and may be deduced from, the identity of the target genes which VGAM235 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14405] Apolipoprotein L, 1 (APOL1, Accession NM_003661) is a VGAM235 host target gene. APOL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL1 BINDING SITE, designated SEQ ID:9732, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14406] A function of VGAM235 is therefore inhibition of Apolipoprotein L, 1 (APOL1, Accession NM_003661), a gene which may participate in reverse cholesterol transport from peripheral cells to the liver. Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL1. The function of APOL1 has been established by previous

studies. By genomic sequence analysis, Page et al. (2001) identified APOL1 within the APOL gene cluster. The predicted 398-amino acid protein has a calculated molecular mass of 43.9 kD. They noted that the APOL proteins share significant identity within the predicted amphipathic alpha helices. Semiquantitative RT-PCR revealed ubiquitous expression of APOL1, with highest levels in lung, spleen, prostate, and placenta, and weak expression in fetal brain and pancreas. In situ hybridization of human placenta revealed expression in all 3 tissue layers, including the basal plate, cytotrophoblast, and chorionic plate. In a microarray analysis of gene expression in the prefrontal cortex of schizophrenia (OMIM Ref. No. 181500) and control brains, Mimmack et al. (2002) found significant upregulation of the APOL1, APOL2 (OMIM Ref. No. 607252), and APOL4 (OMIM Ref. No. 607254) genes.

[14407] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14408] Mimmack, M. L.; Ryan, M.; Baba, H.; Navarro-Ruiz, J.; Iritani, S.; Faull, R. L. M.; McKenna, P. J.; Jones, P. B.; Arai, H.; Starkey, M.; Emson, P. C.; Bahn, S. : Gene expression analysis in schizophrenia: reproducible up-regulation of sev-

eral members of the apolipoprotein L family located in a high-susceptibility locus for schizophrenia on chromosome 22. Proc. Nat. Acad. Sci. 99: 4680–4685, 2002. ; and

- [14409] Page, N. M.; Butlin, D. J.; Lomthaisong, K.; Lowry, P. J. : The human apolipoprotein L gene cluster: identification, classification, and sites of distribution. Genomics 74: 71–78, 200.
- [14410] Further studies establishing the function and utilities of APOL1 are found in John Hopkins OMIM database record ID 603743, and in cited publications numbered 2899–290 and 4884–2902 listed in the bibliography section herein–below, which are also hereby incorporated by reference. 24-dehydrocholesterol Reductase (DHCR24, Accession NM_014762) is another VGAM235 host target gene. DHCR24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DHCR24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DHCR24 BINDING SITE, designated SEQ ID:16528, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ

ID:2946.

[14411] Another function of VGAM235 is therefore inhibition of 24-dehydrocholesterol Reductase (DHCR24, Accession NM_014762), a gene which catalyzes the reduction of sterol intermediates. Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DHCR24. The function of DHCR24 has been established by previous studies. Sarkar et al. (2001) showed that the gene encoding seladin-1, a human homolog of the Diminuto/Dwarf1 gene described in plants and *C. elegans*, has adenoma-specific overexpression. Northern blot analysis revealed that seladin-1 mRNA was overexpressed in the adenoma tissue of 14 patients with Cushing syndrome in comparison to the adjacent nontumorous adrenal gland. In situ hybridization using a seladin-1 cRNA probe showed its abundant expression in the tumor cells, whereas the nontumorous cells showed a low level of expression. Almost no apoptotic cell was detected in the tumor or in the normal adrenal cortex where seladin-1 expression was abundant. The authors noted that their results were compatible with a recent report that seladin-1 acts as an antiapoptotic factor in neurons (Greeve et al., 2000). In addition,

expression of seladin-1 in the normal adrenal cortex was most abundant in the zona fasciculata, suggesting its possible regulation by ACTH/cAMP. The authors concluded that the overexpression of seladin-1 in the adenoma could be due to the abundant expression of ACTH receptor and hypothesized that seladin-1 might be involved in the molecular events of adrenocortical tumorigenesis by facilitating steroid synthesis and cell growth. In a severely affected infant with desmosterolosis (OMIM Ref. No. 602398), Waterham et al. (2001) identified 3 mutations in the DHCR24 gene. The mutation inherited from the mother was a 1412A→C change resulting in a tyr471→ser (Y471S) substitution. Expression studies in *S. cerevisiae* showed nondetectable activity of this variant, consistent with the severe phenotype of the patient. Two mutations on the same allele were inherited from the father: an 881A→C change resulting in an asn294→thr substitution (N294T), and a 918G→C change resulting in a lys306→asn (K306N) substitution (606418.0002). Expression studies in *S. cerevisiae* of the N294T and K306N variants showed 14.4% and 49.8% of wildtype activity, respectively. Expression studies in *S. cerevisiae* of an allele with both mutations from the father showed less than 1%

of wildtype activity. To determine whether one of the mutations inherited from the father was a common polymorphic variant, 50 alleles of controls were analyzed but neither mutation was detected.

[14412] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14413] Sarkar, D.; Imai, T.; Kambe, F.; Shibata, A.; Ohmori, S.; Siddiq, A.; Hayasaka, S.; Funahashi, H.; Seo, H. : The human homolog of Diminuto/Dwarf1 gene (hDiminuto): a novel ACTH-responsive gene overexpressed in benign cortisol-producing adrenocortical adenomas. J. Clin. Endocr. Metab. 86: 5130–5137, 2001. ; and

[14414] Greeve, I.; Hermans-Borgmeyer, I.; Brellinger, C.; Kasper, D.; Gomez-Isla, T.; Behl, C.; Levkau, B.; Nitsch, R. M. : The human DIMINUTO/DWARF1 homolog seladin-1 confers resistance to A.

[14415] Further studies establishing the function and utilities of DHCR24 are found in John Hopkins OMIM database record ID 606418, and in cited publications numbered 676 and 6949 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Gamma-glutamyltransferase 2 (GGT2, Accession

XM_057166) is another VGAM235 host target gene. GGT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GGT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGT2 BINDING SITE, designated SEQ ID:36488, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14416] Another function of VGAM235 is therefore inhibition of Gamma-glutamyltransferase 2 (GGT2, Accession XM_057166). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGT2. Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083) is another VGAM235 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22059, to the nucleotide sequence of VGAM235 RNA, herein designated

VGAM RNA, also designated SEQ ID:2946.

[14417] Another function of VGAM235 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. DKFZp434C0328 (Accession NM_017577) is another VGAM235 host target gene. DKFZp434C0328 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434C0328, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434C0328 BINDING SITE, designated SEQ ID:19015, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14418] Another function of VGAM235 is therefore inhibition of DKFZp434C0328 (Accession NM_017577). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434C0328. FLJ21195 (Accession NM_022469) is another VGAM235 host target gene. FLJ21195 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21195 BINDING SITE, designated SEQ ID:22825, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14419] Another function of VGAM235 is therefore inhibition of FLJ21195 (Accession NM_022469). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21195. MEGF11 (Accession NM_032445) is another VGAM235 host target gene. MEGF11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MEGF11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF11 BINDING SITE, designated SEQ ID:26205, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14420] Another function of VGAM235 is therefore inhibition of

MEGF11 (Accession NM_032445). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEGF11. LOC153937 (Accession XM_087813) is another VGAM235 host target gene. LOC153937 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39449, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14421] Another function of VGAM235 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153937. LOC85414 (Accession NM_033102) is another VGAM235 host target gene. LOC85414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC85414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC85414 BINDING SITE, designated SEQ ID:26954, to the nucleotide sequence of VGAM235 RNA, herein designated VGAM RNA, also designated SEQ ID:2946.

[14422] Another function of VGAM235 is therefore inhibition of LOC85414 (Accession NM_033102). Accordingly, utilities of VGAM235 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC85414. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 236 (VGAM236) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14423] VGAM236 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM236 was detected is described hereinabove with reference to Figs. 1–8.

[14424] VGAM236 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[14425] VGAM236 gene encodes a VGAM236 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM236 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM236 precursor RNA is designated SEQ ID:222, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:222 is located at position 88403 relative to the genome of Calitrichine Herpesvirus 3.

[14426] VGAM236 precursor RNA folds onto itself, forming VGAM236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14427] An enzyme complex designated DICER COMPLEX, `dices` the VGAM236 folded precursor RNA into VGAM236 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 66%) nucleotide sequence of VGAM236 RNA is designated SEQ ID:2947, and is provided hereinbelow with reference to the sequence listing part.

[14428] VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM236 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14429] VGAM236 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM236 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM236 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14430] The complementary binding of VGAM236 RNA, herein designated VGAM RNA, to host target binding sites on VGAM236 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM236 host target RNA into VGAM236 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14431] It is appreciated that VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM236 host target genes. The mRNA of each one of this plurality of VGAM236 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM236 RNA, herein designated VGAM RNA, and which when bound by VGAM236 RNA causes inhibition of translation of respective one or more VGAM236 host target proteins.

[14432] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM236 gene, herein designated VGAM GENE, on one or more VGAM236 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14433] It is yet further appreciated that a function of VGAM236 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM236 correlate with, and may be deduced from, the identity of the host target genes which VGAM236 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14434] Nucleotide sequences of the VGAM236 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM236 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM236 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM236 are further described hereinbelow with reference to Table 1.

[14435] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM236 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM236 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14436] As mentioned hereinabove with reference to Fig. 1, a function of VGAM236 gene, herein designated VGAM is inhibition of expression of VGAM236 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM236 correlate with, and may be deduced from, the identity of the target genes which VGAM236 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14437] V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_005157) is a VGAM236 host target gene. ABL1 BINDING SITE1 and ABL1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABL1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABL1 BINDING SITE1 and ABL1 BINDING SITE2, designated SEQ ID:11636 and SEQ ID:14225 respectively, to the nucleotide sequence of

VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14438] A function of VGAM236 is therefore inhibition of V-abl Abelson Murine Leukemia Viral Oncogene Homolog 1 (ABL1, Accession NM_005157). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABL1. Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281) is another VGAM236 host target gene. SCN1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCN1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN1A BINDING SITE, designated SEQ ID:42828, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14439] Another function of VGAM236 is therefore inhibition of Sodium Channel, Voltage-gated, Type I, Alpha Polypeptide (SCN1A, Accession XM_114281). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN1A.

Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919) is another VGAM236 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:17174, SEQ ID:28438 and SEQ ID:28455 respectively, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14440] Another function of VGAM236 is therefore inhibition of Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_014919), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.Synaptojanin 2 (SYNJ2, Accession XM_029746) is another VGAM236 host target gene. SYNJ2 BINDING SITE

is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYNJ2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYNJ2 BINDING SITE, designated SEQ ID:30940, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14441] Another function of VGAM236 is therefore inhibition of Synaptojanin 2 (SYNJ2, Accession XM_029746). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYNJ2. Synaptotagmin XIII (SYT13, Accession XM_167880) is another VGAM236 host target gene. SYT13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SYT13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SYT13 BINDING SITE, designated SEQ ID:44884, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14442] Another function of VGAM236 is therefore inhibition of

Synaptotagmin XIII (SYT13, Accession XM_167880). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SYT13. LOC152698 (Accession XM_017241) is another VGAM236 host target gene. LOC152698 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152698, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152698 BINDING SITE, designated SEQ ID:30311, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14443] Another function of VGAM236 is therefore inhibition of LOC152698 (Accession XM_017241). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152698. LOC157280 (Accession XM_058301) is another VGAM236 host target gene. LOC157280 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC157280 BINDING SITE, designated SEQ ID:36590, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14444] Another function of VGAM236 is therefore inhibition of LOC157280 (Accession XM_058301). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157280. LOC255448 (Accession XM_170623) is another VGAM236 host target gene. LOC255448 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255448, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255448 BINDING SITE, designated SEQ ID:45400, to the nucleotide sequence of VGAM236 RNA, herein designated VGAM RNA, also designated SEQ ID:2947.

[14445] Another function of VGAM236 is therefore inhibition of LOC255448 (Accession XM_170623). Accordingly, utilities of VGAM236 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255448. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 237 (VGAM237) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14446] VGAM237 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM237 was detected is described hereinabove with reference to Figs. 1–8.

[14447] VGAM237 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14448] VGAM237 gene encodes a VGAM237 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM237 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM237 precursor RNA is designated SEQ ID:223, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:223 is

located at position 74899 relative to the genome of Calitrichine Herpesvirus 3.

[14449] VGAM237 precursor RNA folds onto itself, forming VGAM237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14450] An enzyme complex designated DICER COMPLEX, `dices` the VGAM237 folded precursor RNA into VGAM237 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM237 RNA is designated SEQ ID:2948, and is provided hereinbelow with reference to the sequence listing part.

[14451] VGAM237 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM237 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[14452] VGAM237 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM237 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM237 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM237 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[14453] The complementary binding of VGAM237 RNA, herein designated VGAM RNA, to host target binding sites on VGAM237 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM237 host target RNA into VGAM237 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14454] It is appreciated that VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM237 host target genes. The mRNA of each one of this plurality of VGAM237 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM237 RNA, herein designated VGAM RNA, and which when bound by VGAM237 RNA causes inhibition of translation of respective one or more VGAM237

host target proteins.

[14455] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM237 gene, herein designated VGAM GENE, on one or more VGAM237 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14456] It is yet further appreciated that a function of VGAM237 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3.

Specific functions, and accordingly utilities, of VGAM237 correlate with, and may be deduced from, the identity of the host target genes which VGAM237 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [14457] Nucleotide sequences of the VGAM237 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM237 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM237 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM237 are further described hereinbelow with reference to Table 1.
- [14458] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM237 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM237 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [14459] As mentioned hereinabove with reference to Fig. 1, a function of VGAM237 gene, herein designated VGAM is inhibition of expression of VGAM237 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM237 correlate with, and may be deduced from, the identity of the target genes which VGAM237 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14460] Chemokine-like Receptor 1 (CMKLR1, Accession NM_004072) is a VGAM237 host target gene. CMKLR1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CMKLR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMKLR1 BINDING SITE, designated SEQ ID:10276, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14461] A function of VGAM237 is therefore inhibition of Chemokine-like Receptor 1 (CMKLR1, Accession NM_004072), a gene which may have a function in bone metabolism. Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMKLR1. The function of CMKLR1 has been established by previous studies. Chemokines, a family of small cytokines, recruit leuko-

cytes during inflammation and immune responses.

Chemokine receptors, such as the somatostatin receptors (see, OMIM Ref. No., e.g., 182451), belong to the family of 7-transmembrane G protein-coupled receptors. Gantz et al. (1996) cloned CMKLR1 by PCR of genomic DNA with degenerate primers based on the conserved regions of somatostatin receptors 1–4. The predicted 371-amino acid protein has 7 hydrophobic domains. The CMKLR1 gene has over 40% nucleotide sequence homology to the somatostatin receptors 1–4 and over 50% to IL81R (OMIM Ref. No. 146929) and FPR1 (OMIM Ref. No. 136537).

Northern blot analysis revealed expression of multiple transcripts of different size in all tissues examined. Gantz et al. (1996) mapped the CMKLR1 gene to chromosome 12q24.1 by fluorescence in situ hybridization. While attempting to identify new neuropeptide receptors from a neuroblastoma x glioma cell line by RT-PCR with primers based on conserved regions of G protein-coupled neuropeptide receptors, Methner et al. (1997) cloned a mouse *Cmk1r1* cDNA, which they designated *Dez*. Using in situ hybridization, Methner et al. (1997) found that *Dez* is differentially regulated during mouse development, with prominent expression in developing osseous and carti-

luginous tissues. Owman et al. (1997) cloned the rat homolog, which they designated Cmkrl3, from a liver cDNA library. Using in situ hybridization, they found that Cmkrl3 is widely expressed in the brain and periphery, particularly in cardiovascular elements

[14462] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14463] Gantz, I.; Konda, Y.; Yang, Y.-K.; Miller, D. E.; Dierick, H. A.; Yamada, T. : Molecular cloning of a novel receptor (CMKLR1) with homology to the chemotactic factor receptors. Cytogenet. Cell Genet. 74: 286–290, 1996. ; and

[14464] Methner, A.; Hermey, G.; Schinke, B.; Hermans-Borgmeyer, I. : A novel G protein-coupled receptor with homology to neuropeptide and chemoattractant receptors expressed during bone develop.

[14465] Further studies establishing the function and utilities of CMKLR1 are found in John Hopkins OMIM database record ID 602351, and in cited publications numbered 1015–101 and 1018 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibroblast Growth Factor 23 (FGF23, Accession NM_020638) is another VGAM237 host target gene.

FGF23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF23 BINDING SITE, designated SEQ ID:21790, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14466] Another function of VGAM237 is therefore inhibition of Fibroblast Growth Factor 23 (FGF23, Accession NM_020638), a gene which is a member of the fibroblast growth factor family. Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF23. The function of FGF23 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Pim-1 Oncogene (PIM1, Accession XM_165800) is another VGAM237 host target gene. PIM1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PIM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIM1 BINDING SITE, designated SEQ ID:43755, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14467] Another function of VGAM237 is therefore inhibition of Pim-1 Oncogene (PIM1, Accession XM_165800), a gene which is a protooncogene. Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIM1. The function of PIM1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM95. Thrombomodulin (THBD, Accession NM_000361) is another VGAM237 host target gene. THBD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by THBD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBD BINDING SITE, designated SEQ ID:5921, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14468] Another function of VGAM237 is therefore inhibition of Thrombomodulin (THBD, Accession NM_000361). Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBD. KIAA1056 (Accession NM_014894) is another VGAM237 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17044, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14469] Another function of VGAM237 is therefore inhibition of KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. LOC118786 (Accession XM_061147) is another VGAM237 host target gene. LOC118786 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC118786, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118786 BINDING SITE, designated SEQ ID:37198, to the nucleotide sequence of VGAM237 RNA, herein designated VGAM RNA, also designated SEQ ID:2948.

[14470] Another function of VGAM237 is therefore inhibition of LOC118786 (Accession XM_061147). Accordingly, utilities of VGAM237 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118786. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 238 (VGAM238) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14471] VGAM238 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM238 was detected is described hereinabove with reference to Figs. 1-8.

[14472] VGAM238 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM238 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[14473] VGAM238 gene encodes a VGAM238 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM238 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM238 precursor RNA is designated SEQ ID:224, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:224 is located at position 31365 relative to the genome of Calitrichine Herpesvirus 3.

[14474] VGAM238 precursor RNA folds onto itself, forming VGAM238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14475] An enzyme complex designated DICER COMPLEX, `dices` the VGAM238 folded precursor RNA into VGAM238 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM238 RNA is designated SEQ ID:2949, and is provided hereinbelow with reference to the sequence listing part.

[14476] VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM238 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14477] VGAM238 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM238 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM238 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14478] The complementary binding of VGAM238 RNA, herein designated VGAM RNA, to host target binding sites on VGAM238 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM238 host target RNA into VGAM238 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[14479] It is appreciated that VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM238 host target genes. The mRNA of each one of this plurality of VGAM238 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM238 RNA, herein designated VGAM RNA, and which when bound by VGAM238 RNA causes inhibition of translation of respective one or more VGAM238 host target proteins.

[14480] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM238 gene, herein designated VGAM GENE, on one or more VGAM238 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14481] It is yet further appreciated that a function of VGAM238 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM238 correlate with, and may be deduced from, the identity of the host target genes which VGAM238 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14482] Nucleotide sequences of the VGAM238 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM238 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM238 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM238 are further described hereinbelow with reference to Table 1.

[14483] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM238 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM238 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14484] As mentioned hereinabove with reference to Fig. 1, a function of VGAM238 gene, herein designated VGAM is inhibition of expression of VGAM238 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM238 correlate with, and may be deduced from, the identity of the target genes which VGAM238 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14485] KIAA0441 (Accession NM_014797) is a VGAM238 host target gene. KIAA0441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0441 BINDING SITE, designated SEQ ID:16706, to the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2949.

[14486] A function of VGAM238 is therefore inhibition of KIAA0441 (Accession NM_014797). Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0441. KIAA0481 (Accession XM_050144) is another VGAM238 host target gene. KIAA0481 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0481 BINDING SITE, designated SEQ ID:35566, to the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, also designated SEQ ID:2949.

[14487] Another function of VGAM238 is therefore inhibition of KIAA0481 (Accession XM_050144). Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0481. KIAA0721 (Accession XM_171125) is another VGAM238 host target gene. KIAA0721 BINDING SITE1 and KIAA0721 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by

KIAA0721, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0721 BINDING SITE1 and KIAA0721 BINDING SITE2, designated SEQ ID:45923 and SEQ ID:22316 respectively, to the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, also designated SEQ ID:2949.

[14488] Another function of VGAM238 is therefore inhibition of KIAA0721 (Accession XM_171125). Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0721. LOC131870 (Accession XM_059544) is another VGAM238 host target gene. LOC131870 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC131870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131870 BINDING SITE, designated SEQ ID:37014, to the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, also designated SEQ ID:2949.

[14489] Another function of VGAM238 is therefore inhibition of

LOC131870 (Accession XM_059544). Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131870. LOC202018 (Accession XM_114420) is another VGAM238 host target gene. LOC202018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202018 BINDING SITE, designated SEQ ID:42957, to the nucleotide sequence of VGAM238 RNA, herein designated VGAM RNA, also designated SEQ ID:2949.

[14490] Another function of VGAM238 is therefore inhibition of LOC202018 (Accession XM_114420). Accordingly, utilities of VGAM238 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202018. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 239 (VGAM239) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[14491] VGAM239 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM239 was detected is described hereinabove with reference to Figs. 1–8.

[14492] VGAM239 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14493] VGAM239 gene encodes a VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM239 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM239 precursor RNA is designated SEQ ID:225, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:225 is located at position 83602 relative to the genome of Callitrichine Herpesvirus 3.

[14494] VGAM239 precursor RNA folds onto itself, forming VGAM239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[14495] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM239 folded precursor RNA into VGAM239 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM239 RNA is designated SEQ ID:2950, and
is provided hereinbelow with reference to the sequence
listing part.

[14496] VGAM239 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM239 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM239 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[14497] VGAM239 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM239 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM239 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[14498] The complementary binding of VGAM239 RNA, herein designated VGAM RNA, to host target binding sites on VGAM239 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM239 host target RNA into VGAM239 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14499] It is appreciated that VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM239 host target genes. The mRNA of each one of this plurality of VGAM239 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM239 RNA, herein designated VGAM RNA, and which when bound by VGAM239 RNA causes inhibition of translation of respective one or more VGAM239 host target proteins.

[14500] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM239 gene, herein designated VGAM GENE, on one or

more VGAM239 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14501] It is yet further appreciated that a function of VGAM239 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM239 correlate with, and may be deduced from, the identity of the host target genes which VGAM239 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14502] Nucleotide sequences of the VGAM239 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM239 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM239 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM239 are further described hereinbelow with reference to Table 1.

[14503] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM239 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM239 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14504] As mentioned hereinabove with reference to Fig. 1, a function of VGAM239 gene, herein designated VGAM is inhibition of expression of VGAM239 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM239 correlate with, and may be deduced from, the identity of the target genes which VGAM239 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14505] Neurocalcin Delta (NCALD, Accession NM_032041) is a

VGAM239 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25741, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also designated SEQ ID:2950.

[14506] A function of VGAM239 is therefore inhibition of Neuro-calcin Delta (NCALD, Accession NM_032041). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270) is another VGAM239 host target gene. C20orf20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf20 BINDING SITE, designated SEQ ID:20243, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2950.

[14507] Another function of VGAM239 is therefore inhibition of Chromosome 20 Open Reading Frame 20 (C20orf20, Accession NM_018270). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf20. DKFZP434I0714 (Accession XM_098247) is another VGAM239 host target gene. DKFZP434I0714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434I0714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I0714 BINDING SITE, designated SEQ ID:41527, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also designated SEQ ID:2950.

[14508] Another function of VGAM239 is therefore inhibition of DKFZP434I0714 (Accession XM_098247). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I0714. DKFZP564L0862 (Accession NM_024087) is another VGAM239 host target gene. DKFZP564L0862 BINDING SITE is HOST TARGET binding site

found in the 5` untranslated region of mRNA encoded by DKFZP564L0862, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564L0862 BINDING SITE, designated SEQ ID:23530, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also designated SEQ ID:2950.

[14509] Another function of VGAM239 is therefore inhibition of DKFZP564L0862 (Accession NM_024087). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564L0862. KIAA1649 (Accession NM_032311) is another VGAM239 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1649 BINDING SITE, designated SEQ ID:26101, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also designated SEQ ID:2950.

[14510] Another function of VGAM239 is therefore inhibition of

KIAA1649 (Accession NM_032311). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. PR Domain Containing 15 (PRDM15, Accession XM_029600) is another VGAM239 host target gene. PRDM15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM15 BINDING SITE, designated SEQ ID:30915, to the nucleotide sequence of VGAM239 RNA, herein designated VGAM RNA, also designated SEQ ID:2950.

[14511] Another function of VGAM239 is therefore inhibition of PR Domain Containing 15 (PRDM15, Accession XM_029600). Accordingly, utilities of VGAM239 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM15. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 240 (VGAM240) viral gene, which modulates expression of respective host tar-

get genes thereof, the function and utility of which host target genes is known in the art.

[14512] VGAM240 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM240 was detected is described hereinabove with reference to Figs. 1–8.

[14513] VGAM240 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14514] VGAM240 gene encodes a VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM240 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM240 precursor RNA is designated SEQ ID:226, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:226 is located at position 32744 relative to the genome of Callitrichine Herpesvirus 3.

[14515] VGAM240 precursor RNA folds onto itself, forming VGAM240 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[14516] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM240 folded precursor RNA into VGAM240 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM240 RNA is designated SEQ ID:2951, and
is provided hereinbelow with reference to the sequence
listing part.

[14517] VGAM240 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM240 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM240 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14518] VGAM240 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM240 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM240 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14519] The complementary binding of VGAM240 RNA, herein designated VGAM RNA, to host target binding sites on VGAM240 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM240 host target RNA into VGAM240 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14520] It is appreciated that VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM240 host target genes. The mRNA of each one of this plurality of VGAM240 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM240 RNA, herein designated VGAM RNA, and which when bound by VGAM240 RNA causes inhibition of translation of respective one or more VGAM240 host target proteins.

[14521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM240 gene, herein designated VGAM GENE, on one or more VGAM240 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14522] It is yet further appreciated that a function of VGAM240 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM240 correlate with, and may be deduced from, the identity of the host target genes which VGAM240 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [14523] Nucleotide sequences of the VGAM240 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM240 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM240 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM240 are further described hereinbelow with reference to Table 1.
- [14524] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM240 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM240 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [14525] As mentioned hereinabove with reference to Fig. 1, a function of VGAM240 gene, herein designated VGAM is inhibition of expression of VGAM240 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM240 correlate with, and may be deduced from, the identity of the target genes which VGAM240 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14526] Cell Matrix Adhesion Regulator (CMAR, Accession NM_005200) is a VGAM240 host target gene. CMAR BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CMAR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CMAR BINDING SITE, designated SEQ ID:11698, to the nucleotide sequence of VGAM240 RNA, herein designated VGAM RNA, also designated SEQ ID:2951.

[14527] A function of VGAM240 is therefore inhibition of Cell Matrix Adhesion Regulator (CMAR, Accession NM_005200). Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CMAR. Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_004009) is another VGAM240 host target gene. DMD BINDING SITE1 and DMD BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by DMD, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMD BINDING SITE1 and DMD

BINDING SITE2, designated SEQ ID:10167 and SEQ ID:10173 respectively, to the nucleotide sequence of VGAM240 RNA, herein designated VGAM RNA, also designated SEQ ID:2951.

[14528] Another function of VGAM240 is therefore inhibition of Dystrophin (muscular dystrophy, Duchenne and Becker types) (DMD, Accession NM_004009), a gene which muscular dystrophy . Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DMD. The function of DMD and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM218.MGC22014 (Accession XM_035307) is another VGAM240 host target gene. MGC22014 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC22014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC22014 BINDING SITE, designated SEQ ID:32223, to the nucleotide sequence of VGAM240 RNA, herein designated VGAM RNA, also designated SEQ ID:2951.

[14529] Another function of VGAM240 is therefore inhibition of MGC22014 (Accession XM_035307). Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC22014. Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM_013257) is another VGAM240 host target gene. SGKL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SGKL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SGKL BINDING SITE, designated SEQ ID:14929, to the nucleotide sequence of VGAM240 RNA, herein designated VGAM RNA, also designated SEQ ID:2951.

[14530] Another function of VGAM240 is therefore inhibition of Serum/glucocorticoid Regulated Kinase-like (SGKL, Accession NM_013257). Accordingly, utilities of VGAM240 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SGKL. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 241

(VGAM241) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14531] VGAM241 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM241 was detected is described hereinabove with reference to Figs. 1–8.

[14532] VGAM241 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14533] VGAM241 gene encodes a VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM241 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM241 precursor RNA is designated SEQ ID:227, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:227 is located at position 21896 relative to the genome of Callitrichine Herpesvirus 3.

[14534] VGAM241 precursor RNA folds onto itself, forming

VGAM241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14535] An enzyme complex designated DICER COMPLEX, `dices` the VGAM241 folded precursor RNA into VGAM241 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM241 RNA is designated SEQ ID:2952, and is provided hereinbelow with reference to the sequence listing part.

[14536] VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM241 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14537] VGAM241 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM241 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM241 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14538] The complementary binding of VGAM241 RNA, herein designated VGAM RNA, to host target binding sites on VGAM241 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM241 host target RNA into VGAM241 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14539] It is appreciated that VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM241 host target genes. The mRNA of each one of this plurality of VGAM241 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM241 RNA, herein designated VGAM RNA, and which when bound by VGAM241 RNA causes inhibition of translation of respective one or more VGAM241 host target proteins.

[14540] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM241 gene, herein designated VGAM GENE, on one or more VGAM241 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14541] It is yet further appreciated that a function of VGAM241 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM241 correlate with, and may be deduced from, the identity of the host target genes which VGAM241 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[14542] Nucleotide sequences of the VGAM241 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM241 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM241 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM241 are further described hereinbelow with reference to Table 1.

[14543] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM241 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM241 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14544] As mentioned hereinabove with reference to Fig. 1, a function of VGAM241 gene, herein designated VGAM is inhibition of expression of VGAM241 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM241 correlate with, and may be deduced from, the identity of the target genes which VGAM241 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[14545] Cystinosis, Nephropathic (CTNS, Accession NM_004937) is a VGAM241 host target gene. CTNS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTNS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTNS BINDING SITE, designated SEQ ID:11381, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14546] A function of VGAM241 is therefore inhibition of Cystinosis, Nephropathic (CTNS, Accession NM_004937). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTNS. RAS Guanyl Releasing Protein 1 (calcium and DAG-regulated) (RASGRP1, Accession NM_005739) is another VGAM241 host target gene. RASGRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RASGRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RASGRP1 BINDING SITE, designated SEQ ID:12300, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14547] Another function of VGAM241 is therefore inhibition of RAS Guanyl Releasing Protein 1 (calcium and DAG-regulated) (RASGRP1, Accession NM_005739). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RASGRP1. X-ray Repair Complementing Defective Repair In Chinese Hamster Cells 2 (XRCC2, Accession NM_005431) is another VGAM241 host target gene. XRCC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XRCC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XRCC2 BINDING SITE, designated SEQ ID:11899, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14548] Another function of VGAM241 is therefore inhibition of X-ray Repair Complementing Defective Repair In Chinese

Hamster Cells 2 (XRCC2, Accession NM_005431), a gene which involves in the homologous recombination repair (hrr) pathway of double-stranded dna. Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XRCC2. The function of XRCC2 has been established by previous studies. Johnson et al. (1999) demonstrated that XRCC2 is essential for the efficient repair of DNA double-strand breaks by homologous recombination between sister chromatids. Hamster cells deficient in XRCC2 showed a more than 100-fold decrease in homologous recombination induced by double-strand breaks compared with the parental cell line. This defect was corrected to almost wildtype levels by transient transfection with a plasmid expressing XRCC2. The repair defect in XRCC2 mutant cells appeared to be restricted to recombinational repair because nonhomologous end joining was normal. Johnson et al. (1999) concluded that XRCC2 is involved in the repair of DNA double-strand breaks by homologous recombination. Using a yeast 2-hybrid assay, Braybrooke et al. (2000) identified a direct interaction between XRCC2 and RAD51L3 (OMIM Ref. No. 602954), and they confirmed the interaction by pull-down assays between recombinant

XRCC2 and endogenous RAD51L3 in HeLa cell extracts. Size-exclusion chromatography followed by Western blot analysis suggested that the 2 proteins exist as a heterodimer of about 70 kD.

[14549] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14550] Johnson, R. D.; Liu, N.; Jasin, M. : Mammalian XRCC2 promotes the repair of DNA double-strand breaks by homologous recombination. *Nature* 401: 397–399, 1999. ; and

[14551] Braybrooke, J. P.; Spink, K. G.; Thacker, J.; Hickson, I. D. : The RAD51 family member, RAD51L3, is a DNA-stimulated ATPase that forms a complex with XRCC2. *J. Biol. Chem.* 275: 29100–29.

[14552] Further studies establishing the function and utilities of XRCC2 are found in John Hopkins OMIM database record ID 600375, and in cited publications numbered 1597–1605 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP434O047 (Accession NM_015594) is another VGAM241 host target gene. DKFZP434O047 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP434O047, correspond–

ing to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434O047 BINDING SITE, designated SEQ ID:17858, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14553] Another function of VGAM241 is therefore inhibition of DKFZP434O047 (Accession NM_015594). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434O047. F-box Only Protein 9 (FBXO9, Accession NM_033480) is another VGAM241 host target gene. FBXO9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO9 BINDING SITE, designated SEQ ID:27259, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14554] Another function of VGAM241 is therefore inhibition of F-box Only Protein 9 (FBXO9, Accession NM_033480). Ac-

cordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO9. FLJ21940 (Accession NM_022828) is another VGAM241 host target gene. FLJ21940 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21940 BINDING SITE, designated SEQ ID:23106, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14555] Another function of VGAM241 is therefore inhibition of FLJ21940 (Accession NM_022828). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21940. FLJ22031 (Accession NM_025074) is another VGAM241 host target gene. FLJ22031 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22031 BINDING SITE,

designated SEQ ID:24675, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14556] Another function of VGAM241 is therefore inhibition of FLJ22031 (Accession NM_025074). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22031. Interferon Regulatory Factor 7 (IRF7, Accession NM_004030) is another VGAM241 host target gene. IRF7 BINDING SITE1 through IRF7 BINDING SITE4 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by IRF7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRF7 BINDING SITE1 through IRF7 BINDING SITE4, designated SEQ ID:10250, SEQ ID:7302, SEQ ID:10252 and SEQ ID:10248 respectively, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14557] Another function of VGAM241 is therefore inhibition of Interferon Regulatory Factor 7 (IRF7, Accession NM_004030). Accordingly, utilities of VGAM241 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with IRF7. KIAA1431 (Accession XM_032055) is another VGAM241 host target gene.

KIAA1431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1431 BINDING SITE, designated SEQ ID:31550, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14558] Another function of VGAM241 is therefore inhibition of KIAA1431 (Accession XM_032055). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1431. PP1628 (Accession NM_025201) is another VGAM241 host target gene. PP1628 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP1628, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP1628 BINDING

SITE, designated SEQ ID:24854, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14559] Another function of VGAM241 is therefore inhibition of PP1628 (Accession NM_025201). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP1628. QKI (Accession XM_037438) is another VGAM241 host target gene. QKI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by QKI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of QKI BINDING SITE, designated SEQ ID:32615, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14560] Another function of VGAM241 is therefore inhibition of QKI (Accession XM_037438). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with QKI. Sero-logically Defined Colon Cancer Antigen 33 (SDCCAG33, Accession NM_005786) is another VGAM241 host target gene. SDCCAG33 BINDING SITE is HOST TARGET binding

site found in the 5` untranslated region of mRNA encoded by SDCCAG33, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDCCAG33 BINDING SITE, designated SEQ ID:12369, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14561] Another function of VGAM241 is therefore inhibition of Serologically Defined Colon Cancer Antigen 33 (SDCCAG33, Accession NM_005786). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDCCAG33. Syntrophin (SNPH, Accession NM_014723) is another VGAM241 host target gene. SNPH BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SNPH, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNPH BINDING SITE, designated SEQ ID:16300, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14562] Another function of VGAM241 is therefore inhibition of Syntaphilin (SNPH, Accession NM_014723). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNPH. LOC145644 (Accession XM_035608) is another VGAM241 host target gene. LOC145644 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145644, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145644 BINDING SITE, designated SEQ ID:32288, to the nucleotide sequence of VGAM241 RNA, herein designated VGAM RNA, also designated SEQ ID:2952.

[14563] Another function of VGAM241 is therefore inhibition of LOC145644 (Accession XM_035608). Accordingly, utilities of VGAM241 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145644. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 242 (VGAM242) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[14564] VGAM242 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM242 was detected is described hereinabove with reference to Figs. 1–8.

[14565] VGAM242 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14566] VGAM242 gene encodes a VGAM242 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM242 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM242 precursor RNA is designated SEQ ID:228, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:228 is located at position 102669 relative to the genome of Callitrichine Herpesvirus 3.

[14567] VGAM242 precursor RNA folds onto itself, forming VGAM242 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[14568] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM242 folded precursor RNA into VGAM242 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 49%) nucleotide se-
quence of VGAM242 RNA is designated SEQ ID:2953, and
is provided hereinbelow with reference to the sequence
listing part.

[14569] VGAM242 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM242 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM242 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14570] VGAM242 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM242 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM242 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14571] The complementary binding of VGAM242 RNA, herein designated VGAM RNA, to host target binding sites on VGAM242 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM242 host target RNA into VGAM242 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14572] It is appreciated that VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM242 host target genes. The mRNA of each one of this plurality of VGAM242 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM242 RNA, herein designated VGAM RNA, and which when bound by VGAM242 RNA causes inhibition of translation of respective one or more VGAM242 host target proteins.

[14573] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM242 gene, herein designated VGAM GENE, on one or more VGAM242 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14574] It is yet further appreciated that a function of VGAM242 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM242 correlate with, and may be deduced from, the identity of the host target genes which VGAM242 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [14575] Nucleotide sequences of the VGAM242 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM242 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM242 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM242 are further described hereinbelow with reference to Table 1.
- [14576] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM242 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM242 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [14577] As mentioned hereinabove with reference to Fig. 1, a function of VGAM242 gene, herein designated VGAM is inhibition of expression of VGAM242 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM242 correlate with, and may be deduced from, the identity of the target genes which VGAM242 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14578] Adenylate Cyclase 6 (ADCY6, Accession NM_015270) is a VGAM242 host target gene. ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADCY6, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY6 BINDING SITE1 and ADCY6 BINDING SITE2, designated SEQ ID:17587 and SEQ ID:21975 respectively, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14579] A function of VGAM242 is therefore inhibition of Adenylate Cyclase 6 (ADCY6, Accession NM_015270), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase (by similarity). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY6. The function of ADCY6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM22. Frizzled Homolog 10 (Drosophila) (FZD10, Accession NM_007197) is another VGAM242 host target

gene. FZD10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD10 BINDING SITE, designated SEQ ID:14051, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14580] Another function of VGAM242 is therefore inhibition of Frizzled Homolog 10 (Drosophila) (FZD10, Accession NM_007197). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD10. Homeo Box C4 (HOXC4, Accession NM_014620) is another VGAM242 host target gene. HOXC4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HOXC4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXC4 BINDING SITE, designated SEQ ID:15973, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ

ID:2953.

[14581] Another function of VGAM242 is therefore inhibition of Homeo Box C4 (HOXC4, Accession NM_014620), a gene which is part of a developmental regulatory system that provides cells with specific positional identities on the anterior-posterior axis. Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXC4. The function of HOXC4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM_012266) is another VGAM242 host target gene. DNAJB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAJB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAJB5 BINDING SITE, designated SEQ ID:14588, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14582] Another function of VGAM242 is therefore inhibition of

DnaJ (Hsp40) Homolog, Subfamily B, Member 5 (DNAJB5, Accession NM_012266). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAJB5. DRIL2 (Accession NM_006465) is another VGAM242 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13185, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14583] Another function of VGAM242 is therefore inhibition of DRIL2 (Accession NM_006465). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. KIAA0418 (Accession NM_014631) is another VGAM242 host target gene. KIAA0418 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0418, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0418 BINDING SITE, designated SEQ ID:15996, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14584] Another function of VGAM242 is therefore inhibition of KIAA0418 (Accession NM_014631). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0418. Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM_003559) is another VGAM242 host target gene. PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIP5K2B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2, designated SEQ ID:9608 and SEQ ID:9609 respectively, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14585] Another function of VGAM242 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta

(PIP5K2B, Accession NM_003559). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K2B. Retinoic Acid Induced 15 (RAI15, Accession XM_039548) is another VGAM242 host target gene. RAI15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI15 BINDING SITE, designated SEQ ID:33118, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14586] Another function of VGAM242 is therefore inhibition of Retinoic Acid Induced 15 (RAI15, Accession XM_039548). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI15. SEC14-like 2 (*S. cerevisiae*) (SEC14L2, Accession NM_012429) is another VGAM242 host target gene. SEC14L2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEC14L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC14L2 BINDING SITE, designated SEQ ID:14805, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14587] Another function of VGAM242 is therefore inhibition of SEC14-like 2 (*S. cerevisiae*) (SEC14L2, Accession NM_012429). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC14L2. LOC127534 (Accession XM_060532) is another VGAM242 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37167, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14588] Another function of VGAM242 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC127534. LOC143916 (Accession XM_084664) is another VGAM242 host target gene. LOC143916 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143916, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143916 BINDING SITE, designated SEQ ID:37650, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14589] Another function of VGAM242 is therefore inhibition of LOC143916 (Accession XM_084664). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143916. LOC253917 (Accession XM_171832) is another VGAM242 host target gene. LOC253917 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253917 BINDING SITE, designated SEQ ID:46065, to

the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14590] Another function of VGAM242 is therefore inhibition of LOC253917 (Accession XM_171832). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253917. LOC92568 (Accession XM_045852) is another VGAM242 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34577, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14591] Another function of VGAM242 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. LOC93589 (Accession XM_052387) is another VGAM242 host target gene. LOC93589 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by LOC93589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93589 BINDING SITE, designated SEQ ID:35978, to the nucleotide sequence of VGAM242 RNA, herein designated VGAM RNA, also designated SEQ ID:2953.

[14592] Another function of VGAM242 is therefore inhibition of LOC93589 (Accession XM_052387). Accordingly, utilities of VGAM242 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93589. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 243 (VGAM243) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14593] VGAM243 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM243 was detected is described hereinabove with reference to Figs. 1–8.

[14594] VGAM243 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Callitrichine Herpesvirus 3. VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14595] VGAM243 gene encodes a VGAM243 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM243 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM243 precursor RNA is designated SEQ ID:229, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:229 is located at position 30312 relative to the genome of Callitrichine Herpesvirus 3.

[14596] VGAM243 precursor RNA folds onto itself, forming VGAM243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14597] An enzyme complex designated DICER COMPLEX, `dices` the VGAM243 folded precursor RNA into VGAM243 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM243 RNA is designated SEQ ID:2954, and is provided hereinbelow with reference to the sequence listing part.

[14598] VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM243 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14599] VGAM243 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM243 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM243 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14600] The complementary binding of VGAM243 RNA, herein designated VGAM RNA, to host target binding sites on VGAM243 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM243 host tar-

get RNA into VGAM243 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14601] It is appreciated that VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM243 host target genes. The mRNA of each one of this plurality of VGAM243 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM243 RNA, herein designated VGAM RNA, and which when bound by VGAM243 RNA causes inhibition of translation of respective one or more VGAM243 host target proteins.

[14602] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM243 gene, herein designated VGAM GENE, on one or more VGAM243 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14603] It is yet further appreciated that a function of VGAM243 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM243 correlate with, and may be deduced from, the identity of the host target genes which VGAM243 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14604] Nucleotide sequences of the VGAM243 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM243 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM243 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM243 are further

described hereinbelow with reference to Table 1.

[14605] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM243 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM243 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14606] As mentioned hereinabove with reference to Fig. 1, a function of VGAM243 gene, herein designated VGAM is inhibition of expression of VGAM243 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM243 correlate with, and may be deduced from, the identity of the target genes which VGAM243 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14607] Kinesin Family Member 3C (KIF3C, Accession NM_002254) is a VGAM243 host target gene. KIF3C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIF3C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIF3C BIND-

ING SITE, designated SEQ ID:8060, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14608] A function of VGAM243 is therefore inhibition of Kinesin Family Member 3C (KIF3C, Accession NM_002254). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIF3C. KIAA1828 (Accession XM_057526) is another VGAM243 host target gene. KIAA1828 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA1828, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1828 BINDING SITE, designated SEQ ID:36524, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14609] Another function of VGAM243 is therefore inhibition of KIAA1828 (Accession XM_057526). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1828. Kv6.3 (Accession NM_133490) is another VGAM243 host target gene. Kv6.3 BINDING SITE is HOST

TARGET binding site found in the 3' untranslated region of mRNA encoded by Kv6.3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Kv6.3 BINDING SITE, designated SEQ ID:28564, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14610] Another function of VGAM243 is therefore inhibition of Kv6.3 (Accession NM_133490). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Kv6.3. Matrin 3 (MATR3, Accession NM_018834) is another VGAM243 host target gene. MATR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MATR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MATR3 BINDING SITE, designated SEQ ID:20819, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14611] Another function of VGAM243 is therefore inhibition of

Matrin 3 (MATR3, Accession NM_018834). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MATR3. RRN3 (Accession NM_018427) is another VGAM243 host target gene. RRN3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RRN3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RRN3 BINDING SITE, designated SEQ ID:20486, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14612] Another function of VGAM243 is therefore inhibition of RRN3 (Accession NM_018427). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RRN3. LOC253039 (Accession XM_171203) is another VGAM243 host target gene. LOC253039 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253039, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253039 BINDING SITE, designated SEQ ID:20487, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

tarity of the nucleotide sequences of LOC253039 BINDING SITE, designated SEQ ID:45993, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14613] Another function of VGAM243 is therefore inhibition of LOC253039 (Accession XM_171203). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253039. LOC51634 (Accession NM_016024) is another VGAM243 host target gene. LOC51634 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51634, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51634 BINDING SITE, designated SEQ ID:18100, to the nucleotide sequence of VGAM243 RNA, herein designated VGAM RNA, also designated SEQ ID:2954.

[14614] Another function of VGAM243 is therefore inhibition of LOC51634 (Accession NM_016024). Accordingly, utilities of VGAM243 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51634. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 244 (VGAM244) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14615] VGAM244 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM244 was detected is described hereinabove with reference to Figs. 1–8.

[14616] VGAM244 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14617] VGAM244 gene encodes a VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM244 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM244 precursor RNA is designated SEQ ID:230, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:230 is

located at position 84833 relative to the genome of Calitrichine Herpesvirus 3.

[14618] VGAM244 precursor RNA folds onto itself, forming VGAM244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14619] An enzyme complex designated DICER COMPLEX, `dices` the VGAM244 folded precursor RNA into VGAM244 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM244 RNA is designated SEQ ID:2955, and is provided hereinbelow with reference to the sequence listing part.

[14620] VGAM244 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM244 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[14621] VGAM244 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM244 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM244 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM244 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[14622] The complementary binding of VGAM244 RNA, herein designated VGAM RNA, to host target binding sites on VGAM244 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM244 host target RNA into VGAM244 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14623] It is appreciated that VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM244 host target genes. The mRNA of each one of this plurality of VGAM244 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM244 RNA, herein designated VGAM RNA, and which when bound by VGAM244 RNA causes inhibition of translation of respective one or more VGAM244

host target proteins.

[14624] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM244 gene, herein designated VGAM GENE, on one or more VGAM244 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14625] It is yet further appreciated that a function of VGAM244 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3.

Specific functions, and accordingly utilities, of VGAM244 correlate with, and may be deduced from, the identity of the host target genes which VGAM244 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [14626] Nucleotide sequences of the VGAM244 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM244 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM244 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM244 are further described hereinbelow with reference to Table 1.
- [14627] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM244 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM244 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [14628] As mentioned hereinabove with reference to Fig. 1, a function of VGAM244 gene, herein designated VGAM is inhibition of expression of VGAM244 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM244 correlate with, and may be deduced from, the identity of the target genes which VGAM244 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14629] Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM_012238) is a VGAM244 host target gene. SIRT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SIRT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SIRT1 BINDING SITE, designated SEQ ID:14541, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14630] A function of VGAM244 is therefore inhibition of Sirtuin Silent Mating Type Information Regulation 2 Homolog 1 (*S. cerevisiae*) (SIRT1, Accession NM_012238), a gene which may function as intracellular regulatory protein with mono-ADP-ribosyltransferase activity. Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SIRT1. The function of SIRT1 has been established by pre-

vious studies. Vaziri et al. (2001) showed that the SIRT1 protein binds and deacetylates the p53 protein (OMIM Ref. No. 191170) with a specificity for its C-terminal lys382 residue, modification of which is implicated in the activation of p53 as a transcription factor. Expression of wild-type SIRT1 in human cells reduced the transcriptional activity of p53. In contrast, expression of a catalytically inactive SIRT1 protein potentiated p53-dependent apoptosis and radiosensitivity. These results suggested that SIRT1 is involved in the regulation of p53 function via deacetylation. Luo et al. (2001) showed that mammalian SIRT1 physically interacts with p53 and attenuates p53-mediated functions. Nicotinamide (vitamin B3) inhibited an NAD-dependent p53 deacetylation induced by SIRT1 and also enhanced the p53 acetylation levels in vivo. Furthermore, SIRT1 repressed p53-dependent apoptosis in response to DNA damage and oxidative stress, whereas expression of a SIRT1 point mutant increased the sensitivity of cells in the stress response.

[14631] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14632] Vaziri, H.; Dessain, S. K.; Eaton, E. N.; Imai, S.-I.; Frye, R.

A.; Pandita, T. K.; Guarente, L.; Weinberg, R. A. :
hSIR2-SIRT1 functions as an NAD-dependent p53
deacetylase. Cell 107: 149-159, 2001. ; and

[14633] Luo, J.; Nikolaev, A. Y.; Imai, S.; Chen, D.; Su, F.; Shiloh, A.;
Guarente, L.; Gu, W. : Negative control of p53 by
Sir2-alpha promotes cell survival under stress. Cell 107:
137-148, 2.

[14634] Further studies establishing the function and utilities of
SIRT1 are found in John Hopkins OMIM database record ID
604479, and in cited publications numbered 5008-5010,
504 and 5049-5052 listed in the bibliography section
hereinbelow, which are also hereby incorporated by refer-
ence. Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession
NM_015394) is another VGAM244 host target gene.
ZNF10 BINDING SITE is HOST TARGET binding site found
in the 3' untranslated region of mRNA encoded by ZNF10,
corresponding to a HOST TARGET binding site such as
BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2
illustrates the complementarity of the nucleotide se-
quences of ZNF10 BINDING SITE, designated SEQ
ID:17692, to the nucleotide sequence of VGAM244 RNA,
herein designated VGAM RNA, also designated SEQ
ID:2955.

[14635] Another function of VGAM244 is therefore inhibition of Zinc Finger Protein 10 (KOX 1) (ZNF10, Accession NM_015394), a gene which may function as a transcriptional regulator. Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF10. The function of ZNF10 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM36. Rho Guanine Nucleotide Exchange Factor (GEF) 11 (ARHGEF11, Accession NM_014784) is another VGAM244 host target gene. ARHGEF11 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGEF11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF11 BINDING SITE, designated SEQ ID:16639, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14636] Another function of VGAM244 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 11 (ARHGEF11, Accession NM_014784). Accordingly, utilities

of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF11. Low Density Lipoprotein-related Protein 1B (deleted in tumors) (LRP1B, Accession NM_018557) is another VGAM244 host target gene. LRP1B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LRP1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LRP1B BINDING SITE, designated SEQ ID:20637, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14637] Another function of VGAM244 is therefore inhibition of Low Density Lipoprotein-related Protein 1B (deleted in tumors) (LRP1B, Accession NM_018557). Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LRP1B. Retinoic Acid Induced 15 (RAI15, Accession XM_039548) is another VGAM244 host target gene. RAI15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAI15, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAI15 BINDING SITE, designated SEQ ID:33117, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14638] Another function of VGAM244 is therefore inhibition of Retinoic Acid Induced 15 (RAI15, Accession XM_039548). Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAI15. SDF1 (Accession XM_165565) is another VGAM244 host target gene. SDF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDF1 BINDING SITE, designated SEQ ID:43687, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14639] Another function of VGAM244 is therefore inhibition of SDF1 (Accession XM_165565). Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDF1.

LOC149373 (Accession XM_086507) is another VGAM244 host target gene. LOC149373 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149373 BINDING SITE, designated SEQ ID:38717, to the nucleotide sequence of VGAM244 RNA, herein designated VGAM RNA, also designated SEQ ID:2955.

[14640] Another function of VGAM244 is therefore inhibition of LOC149373 (Accession XM_086507). Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149373. LOC257464 (Accession XM_116972) is another VGAM244 host target gene. LOC257464 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257464, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257464 BINDING SITE, designated SEQ ID:43160, to the nucleotide sequence of VGAM244 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2955.

[14641] Another function of VGAM244 is therefore inhibition of LOC257464 (Accession XM_116972). Accordingly, utilities of VGAM244 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257464. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 245 (VGAM245) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14642] VGAM245 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM245 was detected is described hereinabove with reference to Figs. 1–8.

[14643] VGAM245 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14644] VGAM245 gene encodes a VGAM245 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM245 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM245 precursor RNA is designated SEQ ID:231, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:231 is located at position 42813 relative to the genome of Calitrichine Herpesvirus 3.

[14645] VGAM245 precursor RNA folds onto itself, forming VGAM245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14646] An enzyme complex designated DICER COMPLEX, `dices` the VGAM245 folded precursor RNA into VGAM245 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 64%) nucleotide sequence of VGAM245 RNA is designated SEQ ID:2956, and is provided hereinbelow with reference to the sequence listing part.

[14647] VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM245 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[14648] VGAM245 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM245 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM245 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14649] The complementary binding of VGAM245 RNA, herein designated VGAM RNA, to host target binding sites on VGAM245 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM245 host target RNA into VGAM245 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14650] It is appreciated that VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM245 host target genes. The mRNA of

each one of this plurality of VGAM245 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM245 RNA, herein designated VGAM RNA, and which when bound by VGAM245 RNA causes inhibition of translation of respective one or more VGAM245 host target proteins.

[14651] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM245 gene, herein designated VGAM GENE, on one or more VGAM245 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[14652] It is yet further appreciated that a function of VGAM245 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM245 correlate with, and may be deduced from, the identity of the host target genes which VGAM245 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14653] Nucleotide sequences of the VGAM245 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM245 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM245 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM245 are further described hereinbelow with reference to Table 1.

[14654] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM245 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM245 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[14655] As mentioned hereinabove with reference to Fig. 1, a function of VGAM245 gene, herein designated VGAM is inhibition of expression of VGAM245 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM245 correlate with, and may be deduced from, the identity of the target genes which VGAM245 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14656] ADP-ribosylation Factor 3 (ARF3, Accession NM_001659) is a VGAM245 host target gene. ARF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARF3 BINDING SITE, designated SEQ ID:7377, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14657] A function of VGAM245 is therefore inhibition of ADP-ribosylation Factor 3 (ARF3, Accession NM_001659). Accordingly, utilities of VGAM245 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with ARF3. FE65L2 (Accession NM_133175) is another VGAM245 host target gene. FE65L2 BINDING SITE1 and FE65L2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FE65L2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FE65L2 BINDING SITE1 and FE65L2 BINDING SITE2, designated SEQ ID:28396 and SEQ ID:28397 respectively, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14658] Another function of VGAM245 is therefore inhibition of FE65L2 (Accession NM_133175), a gene which may modulate the internalization of beta-amyloid precursor protein. Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FE65L2. The function of FE65L2 has been established by previous studies. To identify genes similar to Fe65 (OMIM Ref. No. 602709), Duilio et al. (1998) screened a rat brain cDNA library and isolated a Fe65L2 cDNA encoding a deduced 504-amino acid polypeptide.

Like Fe65 and Fe65L1 (OMIM Ref. No. 602710), the rat Fe65L2 protein contains 2 phosphotyrosine-binding (PTB) domains and a WW domain. Northern blot analysis detected predominant expression of a 2-kb Fe65L2 mRNA in rat brain and testis. Using the rat cDNA fragment as probe, Tanahashi and Tabira (1999) cloned human Fe65L2 from a fetal brain cDNA library. Fe65L2 encodes a deduced 486-amino acid protein that shares 86% sequence identity with the rat protein. Using RT-PCR of human fetal brain mRNA, Tanahashi and Tabira (1999) also identified a variant, caused by the splicing of a 6-nucleotide mini-exon, that results results in a peptide lacking 2 amino acids in the first PTB domain. Northern blot analysis revealed expression of a 2.2-kb transcript expressed mainly in the brain and in all brain regions tested. A 2.9-kb transcript was found in other tissues, with strongest expression in pancreas. By radiation hybrid analysis, Tanahashi and Tabira (1999) mapped the FE65L2 gene to chromosome 5.

[14659] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14660] Duilio, A.; Faraonio, R.; Minopoli, G.; Zambrano, N.; Russo,

T. : Fe65L2: a new member of the Fe65 protein family interacting with the intracellular domain of the Alzheimer's beta-amyloid precursor protein. *Biochem. J.* 330: 513-519, 1998. ; and

[14661] Tanahashi, H.; Tabira, T. : Genome structure and chromosomal mapping of the gene for Fe65L2 interacting with Alzheimer's beta-amyloid precursor protein. *Biochem. Biophys. Res. Commun.* 25.

[14662] Further studies establishing the function and utilities of FE65L2 are found in John Hopkins OMIM database record ID 602711, and in cited publications numbered 1120-1122 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563) is another VGAM245 host target gene. SEDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEDL BINDING SITE, designated SEQ ID:15902, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14663] Another function of VGAM245 is therefore inhibition of Spondyloepiphyseal Dysplasia, Late (SEDL, Accession NM_014563), a gene which may play role in vesicular transport from endoplasmic reticulum to golgi. Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEDL. The function of SEDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Sel-1 Suppressor of Lin-12-like (C. elegans) (SEL1L, Accession NM_005065) is another VGAM245 host target gene. SEL1L BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEL1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEL1L BINDING SITE, designated SEQ ID:11500, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14664] Another function of VGAM245 is therefore inhibition of Sel-1 Suppressor of Lin-12-like (C. elegans) (SEL1L, Accession NM_005065), a gene which may play a role in

notch signaling (by similarity). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEL1L. The function of SEL1L has been established by previous studies. Biunno et al. (1997) isolated a novel cDNA, designated SEL1L by them, that shows sequence similarities to sel-1, a gene identified as an extragenic suppressor of the lin-12 hypomorphic mutant from *C. elegans* (3,4:Grant and Greenwald, 1996, 1997). SEL1L exhibited a tissue-specific pattern of expression: high levels of a single 7.5-kb transcript were detected only in the pancreas of healthy individuals, whereas low to undetectable levels were observed in other adult tissues and in some fetal tissues. Because of the tissue-specific expression of the gene, Biunno et al. (1997) studied the gene in human pancreatic carcinomas. They found that 17% of adenocarcinomas of the pancreas did not express SEL1L to a detectable level; however, no gross genomic alterations were apparent within a few hundred kb of the relevant region. By somatic cell hybrid analysis and fluorescence in situ hybridization, Biunno et al. (1997) mapped the SEL1L gene to chromosome 14q31. Donoviel and Bernstein (1999) localized the gene to 14q24.3-q31 by FISH and radiation

hybrid analysis.

[14665] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14666] Biunno, I.; Appierto, V.; Cattaneo, M.; Leone, B. E.; Balzano, G.; Socci, C.; Saccone, S.; Letizia, A.; Valle, G. D.; Sgaramella, V. : Isolation of a pancreas-specific gene located on human chromosome 14q31: expression analysis in human pancreatic ductal carcinomas. *Genomics* 46: 284–286, 1997. ; and

[14667] Donoviel, D. B.; Bernstein, A. : SEL-1L maps to human chromosome 14, near the insulin-dependent diabetes mellitus locus 11. *Genomics* 56: 232–233, 1999.

[14668] Further studies establishing the function and utilities of SEL1L are found in John Hopkins OMIM database record ID 602329, and in cited publications numbered 6003–6006 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10853 (Accession NM_018246) is another VGAM245 host target gene. FLJ10853 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated SEQ ID:20209, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14669] Another function of VGAM245 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. FLJ20511 (Accession NM_017853) is another VGAM245 host target gene. FLJ20511 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20511, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20511 BINDING SITE, designated SEQ ID:19526, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14670] Another function of VGAM245 is therefore inhibition of FLJ20511 (Accession NM_017853). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20511.

KIAA1026 (Accession XM_048825) is another VGAM245 host target gene. KIAA1026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35276, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14671] Another function of VGAM245 is therefore inhibition of KIAA1026 (Accession XM_048825). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. KIAA1198 (Accession XM_032674) is another VGAM245 host target gene. KIAA1198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1198 BINDING SITE, designated SEQ ID:31701, to the nucleotide sequence of VGAM245 RNA, herein designated

VGAM RNA, also designated SEQ ID:2956.

[14672] Another function of VGAM245 is therefore inhibition of KIAA1198 (Accession XM_032674). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1198. KIAA1536 (Accession NM_020898) is another VGAM245 host target gene. KIAA1536 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1536, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1536 BINDING SITE, designated SEQ ID:21921, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14673] Another function of VGAM245 is therefore inhibition of KIAA1536 (Accession NM_020898). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1536. KIAA1615 (Accession XM_044021) is another VGAM245 host target gene. KIAA1615 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1615, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1615 BINDING SITE, designated SEQ ID:34080, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14674] Another function of VGAM245 is therefore inhibition of KIAA1615 (Accession XM_044021). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1615. LOC146227 (Accession XM_085374) is another VGAM245 host target gene. LOC146227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146227 BINDING SITE, designated SEQ ID:38080, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14675] Another function of VGAM245 is therefore inhibition of LOC146227 (Accession XM_085374). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC146227. LOC148137 (Accession NM_144692) is another VGAM245 host target gene. LOC148137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148137 BINDING SITE, designated SEQ ID:29517, to the nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14676] Another function of VGAM245 is therefore inhibition of LOC148137 (Accession NM_144692). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148137. LOC92876 (Accession XM_047739) is another VGAM245 host target gene. LOC92876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92876 BINDING SITE, designated SEQ ID:35039, to the

nucleotide sequence of VGAM245 RNA, herein designated VGAM RNA, also designated SEQ ID:2956.

[14677] Another function of VGAM245 is therefore inhibition of LOC92876 (Accession XM_047739). Accordingly, utilities of VGAM245 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92876. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 246 (VGAM246) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14678] VGAM246 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM246 was detected is described hereinabove with reference to Figs. 1–8.

[14679] VGAM246 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14680] VGAM246 gene encodes a VGAM246 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM246 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM246 precursor RNA is designated SEQ ID:232, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:232 is located at position 84351 relative to the genome of Calitrichine Herpesvirus 3.

[14681] VGAM246 precursor RNA folds onto itself, forming VGAM246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14682] An enzyme complex designated DICER COMPLEX, `dices` the VGAM246 folded precursor RNA into VGAM246 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM246 RNA is designated SEQ ID:2957, and is provided hereinbelow with reference to the sequence listing part.

[14683] VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM246 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[14684] VGAM246 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM246 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM246 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14685] The complementary binding of VGAM246 RNA, herein designated VGAM RNA, to host target binding sites on VGAM246 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM246 host target RNA into VGAM246 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14686] It is appreciated that VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM246 host target genes. The mRNA of each one of this plurality of VGAM246 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM246 RNA, herein designated VGAM RNA, and which when bound by VGAM246 RNA causes inhibition of translation of respective one or more VGAM246 host target proteins.

[14687] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM246 gene, herein designated VGAM GENE, on one or more VGAM246 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[14688] It is yet further appreciated that a function of VGAM246 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM246 correlate with, and may be deduced from, the identity of the host target genes which VGAM246 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14689] Nucleotide sequences of the VGAM246 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM246 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM246 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM246 are further described hereinbelow with reference to Table 1.

[14690] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM246 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM246 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14691] As mentioned hereinabove with reference to Fig. 1, a function of VGAM246 gene, herein designated VGAM is inhibition of expression of VGAM246 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM246 correlate with, and may be deduced from, the identity of the target genes which VGAM246 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14692] Activin A Receptor Type II-like 1 (ACVRL1, Accession NM_000020) is a VGAM246 host target gene. ACVRL1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ACVRL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACVRL1 BINDING SITE, designated SEQ ID:5453, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14693] A function of VGAM246 is therefore inhibition of Activin A Receptor Type II-like 1 (ACVRL1, Accession NM_000020),

a gene which form an heteromeric complex after binding tgf-beta at the cell surface and act as signal transducers. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACVRL1. The function of ACVRL1 has been established by previous studies. Activin A receptor, type II-like kinase 1 (also called activin receptor-like kinase 1) is a type I cell-surface receptor for the TGF-beta super-family of ligands (see OMIM Ref. No. TGF-beta, 190180). It shares with other type I receptors a high degree of similarity in serine-threonine kinase subdomains, a glycine- and serine-rich region (called the GS domain) preceding the kinase domain, and a short C-terminal tail (ten Dijke et al., 1994). The protein (symbolized ALK1 by Johnson et al., 1996) can associate with the TGF-beta or activin type II receptors (OMIM Ref. No. 102581) after cotransfection in COS cells, with the complex binding TGF-beta or activin (see OMIM Ref. No. 147290), respectively. However, the ALK1 ligand in vivo is unknown. Using a polyclonal antibody to ALK1, Abdalla et al. (2000) measured ALK1 expression on human umbilical vein endothelial cells (HUVEC) of newborns from HHT2 families. Animal model experiments lend further support to the function of

ACVRL1. Urness et al. (2000) focused on HHT, wherein arterial and venous beds fail to remain distinct. They generated mice lacking *Acvrl1*, the substance missing in one form of HHT.

[14694] It is appreciated that the abovementioned animal model for ACVRL1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14695] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14696] Johnson, D. W.; Berg, J. N.; Baldwin, M. A.; Gallione, C. J.; Marondel, I.; Yoon, S.-J.; Stenzel, T. T.; Speer, M.; Pericak-Vance, M. A.; Diamond, A.; Guttmacher, A. E.; Jackson, C. E.; Attisano, L.; Kucherlapati, R.; Porteous, M. E. M.; Marchuk, D. A. : Mutations in the activin receptor-like kinase 1 gene in hereditary haemorrhagic telangiectasia type 2. *Nature Genet.* 13: 189–195, 1996. ; and

[14697] Urness, L. D.; Sorensen, L. K.; Li, D. Y. : Arteriovenous malformations in mice lacking activin receptor-like kinase-1. *Nature Genet.* 26: 328–331, 2000.

[14698] Further studies establishing the function and utilities of ACVRL1 are found in John Hopkins OMIM database record

ID 601284, and in cited publications numbered 11919–1334, 10177, 4270, 427 and 6378 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. E2F Transcription Factor 2 (E2F2, Accession NM_004091) is another VGAM246 host target gene. E2F2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by E2F2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of E2F2 BINDING SITE, designated SEQ ID:10293, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14699] Another function of VGAM246 is therefore inhibition of E2F Transcription Factor 2 (E2F2, Accession NM_004091), a gene which binds dna cooperatively with dp proteins and involves in cell cycle regulation. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with E2F2. The function of E2F2 has been established by previous studies. MYC (OMIM Ref. No. 190080) induces transcription of the E2F1, E2F2, and E2F3 (OMIM Ref. No. 600427)

genes. Using primary mouse embryo fibroblasts deleted for individual E2f genes, Leone et al. (2001) showed that MYC-induced S phase and apoptosis requires distinct E2F activities. The ability of Myc to induce S phase was impaired in the absence of either E2f2 or E2f3 but not E2f1 or E2f4 (OMIM Ref. No. 600659). In contrast, the ability of Myc to induce apoptosis was markedly reduced in cells deleted for E2f1 but not E2f2 or E2f3. The authors proposed that the induction of specific E2F activities is an essential component in the MYC pathways that control cell proliferation and cell fate decisions. The retinoblastoma tumor suppressor (Rb) pathway is believed to have a critical role in the control of cellular proliferation by regulating E2F activities. E2F1, E2F2, and E2F3 belong to a subclass of E2F factors thought to act as transcriptional activators important for progression through the G1/S transition. Wu et al. (2001) used a conditional gene targeting approach to demonstrate that combined loss of these 3 E2F factors severely affects E2F target expression and completely abolishes the ability of mouse embryonic fibroblasts to enter S phase, progress through mitosis, and proliferate. Loss of E2F function results in elevation of CIP1 (OMIM Ref. No. 116899) protein, leading to a de-

crease in cyclin-dependent kinase activity and Rb phosphorylation. Wu et al. (2001) concluded that these findings suggest a function for this subclass of E2F transcriptional activators in a positive feedback loop, through downmodulation of CIP1, that leads to the inactivation of Rb-dependent repression and S phase entry. By targeting the entire subclass of E2F transcriptional activators, Wu et al. (2001) provided direct genetic evidence for their essential role in cell cycle progression, proliferation, and development. Wu et al. (2001) initially generated and interbred E2f1, E2f2, and E2f3 mutant mice, and found that although mice null for E2f1 and E2f2 were viable and developed to adulthood, mice null for E2f1 and E2f3 or E2f2 and E2f3 died early during embryonic development, at or just before embryonic day 9.5, pointing to a central role for E2F3 in mouse development.

[14700] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14701] Leone, G.; Sears, R.; Huang, E.; Rempel, R.; Nuckolls, F.; Park, C.-H.; Giangrande, P.; Wu, L.; Saavedra, H. I.; Field, S. J.; Thompson, M. A.; Yang, H.; Fujiwara, Y.; Greenberg, M. E.; Orkin, S.; Smith, C.; Nevins, J. R. : Myc requires dis-

tinct E2F activities to induce S phase and apoptosis.

Molec. Cell 8: 105–113, 2001. ; and

[14702] Wu, L.; Timmers, C.; Maiti, B.; Saavedra, H. I.; Sang, L.; Chong, G. T.; Nuckolls, F.; Giangrande, P.; Wright, F. A.; Field, S. J.; Greenberg, M. E.; Orkin, S.; Nevins, J. R.; Robinson.

[14703] Further studies establishing the function and utilities of E2F2 are found in John Hopkins OMIM database record ID 600426, and in cited publications numbered 7561–756 and 9711 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206) is another VGAM246 host target gene. PDGFRA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDGFRA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRA BINDING SITE, designated SEQ ID:12882, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14704] Another function of VGAM246 is therefore inhibition of

Platelet-derived Growth Factor Receptor, Alpha Polypeptide (PDGFRA, Accession NM_006206), a gene which this receptor binds platelet-derived growth factor and has a tyrosine-protein kinase activity. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRA. The function of PDGFRA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM117. Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400) is another VGAM246 host target gene. PLA2G2D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2G2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2G2D BINDING SITE, designated SEQ ID:14773, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14705] Another function of VGAM246 is therefore inhibition of Phospholipase A2, Group IID (PLA2G2D, Accession NM_012400), a gene which is involved in phospholipid di-

gestion, remodeling of cell membranes, and host defense, as well as pathophysiologic processes. Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2G2D. The function of PLA2G2D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Complexin 1 (CPLX1, Accession NM_006651) is another VGAM246 host target gene. CPLX1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPLX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPLX1 BINDING SITE, designated SEQ ID:13451, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14706] Another function of VGAM246 is therefore inhibition of Complexin 1 (CPLX1, Accession NM_006651). Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPLX1. DKFZP566K1924 (Accession XM_057469) is another VGAM246 host target gene. DKFZP566K1924

BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP566K1924, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566K1924 BINDING SITE, designated SEQ ID:36519, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14707] Another function of VGAM246 is therefore inhibition of DKFZP566K1924 (Accession XM_057469). Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566K1924. PAX Transcription Activation Domain Interacting Protein 1 Like (PAXIP1L, Accession XM_046538) is another VGAM246 host target gene. PAXIP1L BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PAXIP1L, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PAXIP1L BINDING SITE, designated SEQ ID:34739, to the nucleotide sequence of VGAM246 RNA,

herein designated VGAM RNA, also designated SEQ ID:2957.

[14708] Another function of VGAM246 is therefore inhibition of PAX Transcription Activation Domain Interacting Protein 1 Like (PAXIP1L, Accession XM_046538). Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAXIP1L. LOC147791 (Accession XM_097293) is another VGAM246 host target gene. LOC147791 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147791, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147791 BINDING SITE, designated SEQ ID:40858, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14709] Another function of VGAM246 is therefore inhibition of LOC147791 (Accession XM_097293). Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147791. LOC149296 (Accession XM_086481) is another VGAM246 host target gene. LOC149296 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149296, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149296 BINDING SITE, designated SEQ ID:38695, to the nucleotide sequence of VGAM246 RNA, herein designated VGAM RNA, also designated SEQ ID:2957.

[14710] Another function of VGAM246 is therefore inhibition of LOC149296 (Accession XM_086481). Accordingly, utilities of VGAM246 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149296. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 247 (VGAM247) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14711] VGAM247 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM247 was detected is described hereinabove with reference to Figs. 1-8.

[14712] VGAM247 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14713] VGAM247 gene encodes a VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM247 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM247 precursor RNA is designated SEQ ID:233, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:233 is located at position 25823 relative to the genome of Callitrichine Herpesvirus 3.

[14714] VGAM247 precursor RNA folds onto itself, forming VGAM247 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[14715] An enzyme complex designated DICER COMPLEX, `dices` the VGAM247 folded precursor RNA into VGAM247 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM247 RNA is designated SEQ ID:2958, and is provided hereinbelow with reference to the sequence listing part.

[14716] VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM247 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14717] VGAM247 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM247 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM247 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM247 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14718] The complementary binding of VGAM247 RNA, herein designated VGAM RNA, to host target binding sites on VGAM247 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM247 host target RNA into VGAM247 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14719] It is appreciated that VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM247 host target genes. The mRNA of each one of this plurality of VGAM247 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM247 RNA, herein designated VGAM RNA, and which when bound by VGAM247 RNA causes inhibition of translation of respective one or more VGAM247 host target proteins.

[14720] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM247 gene, herein designated VGAM GENE, on one or more VGAM247 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14721] It is yet further appreciated that a function of VGAM247 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM247 correlate with, and may be deduced from, the identity of the host target genes which VGAM247 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14722] Nucleotide sequences of the VGAM247 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM247 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM247 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM247 are further described hereinbelow with reference to Table 1.

[14723] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM247 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM247 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14724] As mentioned hereinabove with reference to Fig. 1, a function of VGAM247 gene, herein designated VGAM is inhibition of expression of VGAM247 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM247 correlate with, and may be deduced from, the identity of the target genes which VGAM247 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14725] Amyloid Beta (A4) Precursor Protein-binding, Family A, Member 1 (X11) (APBA1, Accession XM_046018) is a VGAM247 host target gene. APBA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APBA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APBA1 BINDING SITE, designated SEQ ID:34647, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14726] A function of VGAM247 is therefore inhibition of Amyloid Beta (A4) Precursor Protein-binding, Family A, Member 1 (X11) (APBA1, Accession XM_046018), a gene which stabilises APP and inhibits production of proteolytic APP fragments. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APBA1. The function of APBA1 has been established by previous studies. Abnormal processing of the membrane-spanning amyloid precursor protein (APP; 104760), resulting in the production of increased amounts of fibrillogenic beta-amyloid peptide (OMIM Ref. No. A-beta), is considered to be one of the key metabolic events underlying Alzheimer disease (OMIM Ref. No. 104300). One pathway for A-beta production involves the reinternalization of membrane-bound APP into lysosomes where APP containing intact A-beta are generated. In common with a number of cell surface receptors, the C-terminal cytoplasmic domain of APP contains an asn-

pro-thr-tyr (NPTY) motif that mediates re-internalization via clathrin-coated pits (Chen et al., 1990). This motif has also been demonstrated to be a consensus sequence for binding to phosphotyrosine-binding/-interacting domain (PTB)-bearing proteins (van der Geer and Pawson, 1995). Several groups demonstrated that the cytoplasmic domain of APP binds to 4 human PTB proteins: X11, X11-like (APBA2; 602712), Fe65 (APBB1; 602709), and Fe65-like (APBB2; 602710). PTB-domain proteins are believed to be involved in signal transduction processes, and the interaction of APP with the 4 human PTB proteins suggest a role for APP in such signal transduction mechanisms. Furthermore, as the 4 proteins interact with the YENPTY motif in APP, these PTB proteins may modulate processing of APP and hence formation of A-beta. Blanco et al. (1998) pointed out that it is generally agreed that there are as yet unidentified susceptibility genes for Alzheimer disease. The genes APBA1, APBA2, APBB1, and APBB2 represent such candidate genes. By searching for proteins that bind to Munc18-1 (OMIM Ref. No. 602926), Okamoto and Sudhof (1997) isolated rat cDNAs encoding Mint1 and Mint2. They determined the full-length human MINT1 cDNA sequence (GenBank AF029106) using human MINT1 ESTs.

The deduced 837–amino acid MINT1 protein contains an N–terminal domain that binds to Munc18–1, a middle phosphotyrosine–binding (PTB) domain that binds to phosphatidylinositol phosphates, and 2 C–terminal PDZ domains. The rat Mint1 protein is largely membrane–bound and copurifies with synaptic plasma membranes, but it is not a component of synaptic vesicles. The authors suggested that in the brain Mint1 is part of a multimeric complex containing Munc18–1 and syntaxin–1 (OMIM Ref. No. 186590) that likely functions as an intermediate in synaptic vesicle docking/fusion.

[14727] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14728] Blanco, G.; Irving, N. G.; Brown, S. D. M.; Miller, C. C. J.; McLoughlin, D. M. : Mapping of the human and murine X11–like genes (APBA2 and Apba2), the murine Fe65 gene (Apbb1), and the human Fe65–like gene (APBB2): genes encoding phosphotyrosine–binding domain proteins that interact with the Alzheimer's disease amyloid precursor protein. *Mammalian Genome* 9: 473–475, 1998. ; and

[14729] Okamoto, M.; Sudhof, T. C. : Mints, Munc18–interacting proteins in synaptic vesicle exocytosis. *J. Biol. Chem.* 272:

31459–31464, 1997.

[14730] Further studies establishing the function and utilities of APBA1 are found in John Hopkins OMIM database record ID 602414, and in cited publications numbered 1019–1023, 9589, 102 and 1455 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Bone Morphogenetic Protein 1 (BMP1, Accession NM_006132) is another VGAM247 host target gene. BMP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BMP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP1 BINDING SITE, designated SEQ ID:12773, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14731] Another function of VGAM247 is therefore inhibition of Bone Morphogenetic Protein 1 (BMP1, Accession NM_006132), a gene which cleaves procollagens leading to formation of extracellular matrix. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP1. The function of BMP1 has been established by previous

studies. The BMP1 locus encodes a protein that is capable of inducing formation of cartilage in vivo (Wozney et al., 1988). Although other bone morphogenetic proteins are members of the TGF-beta (OMIM Ref. No. 190180) superfamily, BMP1 encodes a novel protein that is not closely related to other known growth factors. Kessler et al. (1996) showed that recombinantly expressed BMP1 and purified procollagen C proteinase (PCP), a secreted metalloprotease requiring calcium and needed for cartilage and bone formation, are, in fact, identical. PCP cleaves the C-terminal propeptides of procollagen I (OMIM Ref. No. 120150), II (OMIM Ref. No. 120140), and III (OMIM Ref. No. 120180) and its activity is increased by the procollagen C-endopeptidase enhancer protein (OMIM Ref. No. 600270). Reddi (1996) discussed the significance of the finding that BMP1 is the same as procollagen C-proteinase.

[14732] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14733] Wozney, J. M.; Rosen, V.; Celeste, A. J.; Mitsock, L. M.; Whitters, M. J.; Kriz, R. W.; Hewick, R. M.; Wang, E. A. : Novel regulators of bone formation: molecular clones and

activities. Science 242: 1528–1534, 1988. ; and

[14734] Kessler, E.; Takahara, K.; Biniaminov, L.; Brusel, M.; Greenspan, D. : Bone morphogenic protein–1: the type I procollagen C–proteinase. Science 271: 360–362, 1996.

[14735] Further studies establishing the function and utilities of BMP1 are found in John Hopkins OMIM database record ID 112264, and in cited publications numbered 11640–11643, 1909, 1912, 11629–191 and 11630 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Calpain 10 (CAPN10, Accession NM_023088) is another VGAM247 host target gene. CAPN10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CAPN10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAPN10 BINDING SITE, designated SEQ ID:23354, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14736] Another function of VGAM247 is therefore inhibition of Calpain 10 (CAPN10, Accession NM_023088), a gene which catalyzes limited proteolysis of substrates involved

in cytoskeletal remodelling and signal transduction. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAPN10. The function of CAPN10 has been established by previous studies. The results of Horikawa et al. (2000) suggested a novel pathway involved in the pathophysiology of diabetes, one that may include, in addition to calpain-10, its substrates, inhibitors, and activators. Calpain-10 may represent the third example of a protease contributing to the development of diabetes, the others being prohormone-processing carboxypeptidase E (OMIM Ref. No. 114855) and prohormone convertase-1 (OMIM Ref. No. 162150), both of which are associated with diabetes and obesity. Horikawa et al. (2000) found a single-nucleotide polymorphism (SNP) associated with noninsulin-dependent diabetes mellitus (OMIM Ref. No. 125853). The G/A variation involved nucleotide 4852 of the genomic sequence of the CAPN10 gene and was located in intron 3, 746 bp downstream of the splice donor site and 176 bp upstream of the splice acceptor site. This and 2 other polymorphisms in the CAPN10 gene refined a haplotype that was associated with greatest risk of diabetes in Mexican-Americans, as well as in Finnish and

German populations.

[14737] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14738] Horikawa, Y.; Oda, N.; Cox, N. J.; Li, X.; Orho-Melander, M.; Hara, M.; Hinokio, Y.; Lindner, T. H.; Mashima, H.; Schwarz, P. E. H.; del Bosque-Plata, L.; Horikawa, Y.; and 14 others : Genetic variation in the gene encoding calpain-10 is associated with type 2 diabetes mellitus. *Nature Genet.* 26: 163–175, 2000. ; and

[14739] Hanis, C. L.; Boerwinkle, E.; Chakraborty, R.; Ellsworth, D. L.; Concannon, P.; Stirling, B.; Morrison, V. A.; Wapelhorst, B.; Spielman, R. S.; Gogolin-Ewens, K. J.; Shephard, J. M.; Wi.

[14740] Further studies establishing the function and utilities of CAPN10 are found in John Hopkins OMIM database record ID 605286, and in cited publications numbered 1330–1331, 6979–6981, 698 and 6982–6983 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487) is another VGAM247 host target gene. CDKN2B BINDING SITE is HOST TARGET binding site found

in the 5` untranslated region of mRNA encoded by CDKN2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2B BINDING SITE, designated SEQ ID:27809, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14741] Another function of VGAM247 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2B (p15, inhibits CDK4) (CDKN2B, Accession NM_078487). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2B. Cyclin-dependent Kinase Inhibitor 2D (p19, inhibits CDK4) (CDKN2D, Accession NM_001800) is another VGAM247 host target gene. CDKN2D BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CDKN2D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDKN2D BINDING SITE, designated SEQ ID:7554, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2958.

[14742] Another function of VGAM247 is therefore inhibition of Cyclin-dependent Kinase Inhibitor 2D (p19, inhibits CDK4) (CDKN2D, Accession NM_001800), a gene which interacts strongly with cdk4 and cdk6. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDKN2D. The function of CDKN2D has been established by previous studies. Cyclins are important in regulating the cell cycle through their formation of enzymatic complexes with various cyclin-dependent kinases. The D type cyclins complex with CDK4 (OMIM Ref. No. 123829) and CDK6 to govern progression through the G1 phase of the cell cycle and later are involved with inactivating phosphorylation of the RB protein (OMIM Ref. No. 180200) which results in release of RB-associated transcription factors that are needed for entry into S phase (Okuda et al., 1995). The activity of the cyclin D-dependent kinases is, in part, controlled by inhibitors such as the INK4 family (which includes INK4a (CDKN2A; 600160), 4b (CDKN2B; 600431), 4c (OMIM Ref. No. CDKN2C), and 4d (OMIM Ref. No. CDKN2D)). INK4a has been shown to act by competing with CDK4 and CDK6 and functions as a tumor suppressor

in a variety of cancers. The INK4d protein was first identified in a yeast 2-hybrid system screened for CDK4 binding proteins (Hirai et al., 1995). The mouse INK4d protein interacts with cdk6 as well. In fibroblasts and macrophages it is rapidly induced at the G1-to-S transition. Overexpression of INK4d caused NIH 3T3 cells to arrest in G1 phase and inhibited cyclin D1-CDK4 kinase activity (Hirai et al., 1995). Okuda et al. (1995) described the cloning and mapping of the human INK4d gene (OMIM Ref. No. CDKN2D). The predicted 166-amino acid protein is 86% identical to the mouse protein and about 45% identical to other human INK4 family members. Northern blots showed that the 1.4-kb transcript is ubiquitously expressed with the highest levels in tissues with the most rapidly dividing cells. Lowest expression occurs at mid G1 phase and is highest during S phase. Okuda et al. (1995) obtained a P1-phage genomic clone including the gene and mapped it by fluorescence in situ hybridization to 19p13

[14743] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14744] Hirai, H.; Roussel, M. F.; Kato, J.-Y.; Ashmun, R. A.; Sherr,

C. J. : Novel INK4 proteins, p19 and p18, are specific inhibitors of cyclin D-dependent kinases CDK4 and CDK6. Molec. Cell. Biol. 15: 2672–2681, 1995. ; and

[14745] Okuda, T.; Hirai, H.; Valentine, V. A.; Shurtleff, S. A.; Kidd, V. J.; Lahti, J. M.; Sherr, C. J.; Downing, J. R. : Molecular cloning, expression pattern, and chromosomal localization o.

[14746] Further studies establishing the function and utilities of CDKN2D are found in John Hopkins OMIM database record ID 600927, and in cited publications numbered 6859–6860 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434) is another VGAM247 host target gene. DAAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44330, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14747] Another function of VGAM247 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAAM2. The function of DAAM2 has been established by previous studies. By sequencing randomly selected cDNAs corresponding to relatively long transcripts from brain, Nagase et al. (1997) identified a cDNA which they designated KIAA0381. The KIAA0381 cDNA encodes an 864-amino acid protein predicted to be involved in cell division. RT-PCR analysis detected expression of KIAA0381 in most tissues tested. Wnt (see OMIM Ref. No. 164975) signaling via the frizzled receptor (Fz; OMIM Ref. No. 600667) controls cell polarity and movement during development. Habas et al. (2001) reported that in human cells and during *Xenopus* embryogenesis, Wnt/Fz signaling activates the small GTPase Rho (OMIM Ref. No. 165390), a key regulator of cytoskeleton architecture. Wnt/Fz activation of Rho requires the cytoplasmic protein dishevelled (DVL; OMIM Ref. No. 601365) and a novel formin (see OMIM Ref. No. 136535) homology (FH)

protein that they identified and named DAAM1 (OMIM Ref. No. 606626). Habas et al. (2001) identified DAAM2, which is identical to KIAA0381, as a protein that is closely related to DAAM1.

[14748] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14749] Habas, R.; Kato, Y.; He, X. : Wnt/Frizzled activation of Rho regulates vertebrate gastrulation and requires a novel Formin homology protein Daam1. Cell 107: 843–854, 2001. ; and

[14750] Nagase, T.; Ishikawa, K.; Nakajima, D.; Ohira, M.; Seki, N.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human gene.

[14751] Further studies establishing the function and utilities of DAAM2 are found in John Hopkins OMIM database record ID 606627, and in cited publications numbered 4522 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231) is another VGAM247 host target gene. FLRT2 BINDING SITE is HOST TARGET binding site found in the

3' untranslated region of mRNA encoded by FLRT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLRT2 BINDING SITE, designated SEQ ID:14882, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14752] Another function of VGAM247 is therefore inhibition of Fibronectin Leucine Rich Transmembrane Protein 2 (FLRT2, Accession NM_013231), a gene which may have a function in cell adhesion and/or receptor signaling. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLRT2. The function of FLRT2 has been established by previous studies. The FLRT family of proteins structurally resembles small leucine-rich proteoglycans found in the extracellular matrix. By screening human brain cDNAs for the potential to encode proteins that are at least 50 kD, Ishikawa et al. (1997) isolated a FLRT2 cDNA, which they called KIAA0405. The deduced 660-amino acid full-length FLRT2 protein shares 25% amino acid sequence identity with the precursor of the alpha chain of human platelet glycoprotein Ib (GP1BA; OMIM Ref. No.

231200) across 180 residues. By SDS-PAGE, in vitro transcribed/translated FLRT2 had an apparent molecular mass of approximately 75 kD. RT-PCR detected FLRT2 expression in a number of human tissues, with highest expression in ovary and relatively high expression in brain and pancreas. By searching a human EST database with portions of the FLRT1 protein (OMIM Ref. No. 604806) sequence, Lacy et al. (1999) identified ESTs encoding FLRT2. The full-length FLRT2 coding sequence encodes a predicted 660-amino acid protein containing a putative N-terminal signal sequence, 10 leucine-rich repeats (LRRs) flanked by N- and C-terminal cysteine-rich regions, a fibronectin-/collagen-like domain, a transmembrane domain, and an intracellular C-terminal tail. FLRT2 has 5 potential N-glycosylation sites in its extracellular region. FLRT2 shares 44% amino acid sequence identity with FLRT3 (OMIM Ref. No. 604808) and 41% identity with FLRT1. Recombinant FLRT2 expressed in SF9 insect cells and monkey COS-1 cells migrated as an 85-kD protein on SDS-polyacrylamide gels. The authors demonstrated that FLRT2 is glycosylated. Northern blot analysis of a variety of human adult tissues detected a 7.5-kb FLRT2 transcript that was expressed abundantly in pancreas and less

abundantly in skeletal muscle, brain, and heart. Lacy et al. (1999) suggested that FLRT2 functions in cell adhesion and/or receptor signaling. By analysis of a radiation hybrid mapping panel, Ishikawa et al. (1997) mapped the FLRT2 gene to chromosome 14. Lacy et al. (1999) noted that a UniGene cluster corresponding to the FLRT2 gene has been mapped to 14q24–q32.

[14753] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14754] Ishikawa, K.; Nagase, T.; Nakajima, D.; Seki, N.; Ohira, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. VIII. 78 new cDNA clones from brain which code for large proteins in vitro. DNA Res. 4: 307–313, 1997. ; and

[14755] Lacy, S. E.; Bonnemann, C. G.; Buzney, E. A.; Kunkel, L. M. : Identification of FLRT1, FLRT2, and FLRT3: a novel family of transmembrane leucine-rich repeat proteins. Genomics 62: 417–4.

[14756] Further studies establishing the function and utilities of FLRT2 are found in John Hopkins OMIM database record ID 604807, and in cited publications numbered 110 and

4385 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Glypican 6 (GPC6, Accession NM_005708) is another VGAM247 host target gene. GPC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPC6 BINDING SITE, designated SEQ ID:12261, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14757] Another function of VGAM247 is therefore inhibition of Glypican 6 (GPC6, Accession NM_005708), a gene which may play a role in growth control and differentiation. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPC6. The function of GPC6 has been established by previous studies. By searching an EST database for glypican-related cDNA sequences and using 5-prime RACE on a human fetal brain cDNA library, Veugelers et al. (1999) identified a novel glypican, which they designated glypican-6. The GPC6 gene, which contains 9 exons, en-

codes a 555-amino acid protein with a molecular mass of approximately 65 kD. The GPC6 protein is 63% identical to GPC4 (OMIM Ref. No. 300168). Like all glypicans, GPC6 starts and terminates with signal peptide-like sequences. The N-terminal sequence is predicted to be required for membrane translocation, and the C-terminal sequence supports the temporary membrane anchoring and subsequent glypiation of the protein. A motif that promotes the assembly of heparan sulfate in proteoglycans is also found at the C-terminal end. Northern blot analysis revealed ubiquitous expression of GPC6 in all fetal and nearly all adult tissues, with the exception of thymus and peripheral blood leukocytes. A major mRNA species of 6.2 kb was most abundant in the ovary, with high expression also in liver, kidney, small intestine, and colon (Paine-Saunders et al., 1999; Veugelers et al., 1999). In situ hybridization studies localized glypican-6 predominantly to mesenchymal tissues in the developing mouse embryo. Veugelers et al. (1999) suggested that growth factor signaling in these tissues might be regulated in part by GPC6 on the cell surface. Paine-Saunders et al. (1999) and Veugelers et al. (1999) mapped the GPC6 gene to 13q32 in a tight cluster with GPC5 (OMIM Ref. No.

602446) by radiation hybrid techniques and FISH, respectively. The GPC6/GPC5 cluster is analogous to the GPC3/GPC4 (OMIM Ref. No. 300168) cluster on Xq26.

[14758] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14759] Paine-Saunders, S.; Viviano, B. L.; Saunders, S. : GPC6, a novel member of the glypican gene family, encodes a product structurally related to GPC4 and is colocalized with GPC5 on human chromosome 13. *Genomics* 57: 455-458, 1999. ; and

[14760] Veugelers, M.; De Cat, B.; Ceulemans, H.; Bruystens, A. M.; Coomans, C.; Durr, J.; Vermeesch, J.; Marynen, P.; David, G. : Glypican-6, a new member of the glypican family of cell surfa.

[14761] Further studies establishing the function and utilities of GPC6 are found in John Hopkins OMIM database record ID 604404, and in cited publications numbered 7442-7443 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lamin B Receptor (LBR, Accession XM_001795) is another VGAM247 host target gene. LBR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by LBR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBR BINDING SITE, designated SEQ ID:29853, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14762] Another function of VGAM247 is therefore inhibition of Lamin B Receptor (LBR, Accession XM_001795). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LBR. LFG (Accession XM_084780) is another VGAM247 host target gene. LFG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LFG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LFG BINDING SITE, designated SEQ ID:37696, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14763] Another function of VGAM247 is therefore inhibition of LFG (Accession XM_084780). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with LFG. V-yes-1 Yamaguchi Sarcoma Viral Related Oncogene Homolog (LYN, Accession NM_002350) is another VGAM247 host target gene. LYN BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LYN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LYN BINDING SITE, designated SEQ ID:8154, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14764] Another function of VGAM247 is therefore inhibition of V-yes-1 Yamaguchi Sarcoma Viral Related Oncogene Homolog (LYN, Accession NM_002350), a gene which is a Tyrosine kinase with similarity to murine tyrosine kinase p56lck; similar to v-yes protein and the gene products of v-fgr and v-src. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LYN. The function of LYN has been established by previous studies. Parravicini et al. (2002) noted that Lyn deficiency impairs some mast cell functions, but degranulation and cytokine production are

intact. In Gab2 (OMIM Ref. No. 606203)–deficient mice, on the other hand, degranulation and cytokine production are impaired. Using immunoblot analysis, they showed that although Lyn is essential for Syk (OMIM Ref. No. 600085) activation and Lat (OMIM Ref. No. 602354) phosphorylation after Fc ϵ 1 (see OMIM Ref. No. FCER1G; 147139) aggregation, neither Lyn nor Lat are necessary for Gab2 phosphorylation. RT–PCR and coimmunoprecipitation analyses demonstrated abundant Fyn (OMIM Ref. No. 137025) expression in mast cells and an association with Gab2. In cells lacking Fyn, neither Gab2 nor Akt (OMIM Ref. No. 164730) were phosphorylated. Functional analysis showed that Lyn $-/-$ mast cells exhibited hyperdegranulation and enhanced PI3K (see OMIM Ref. No. 601232) activity and Akt phosphorylation, whereas in Fyn $-/-$ mast cells the degranulation response was inhibited. The inhibition was associated with decreased binding of PI3K with Gab2. Parravicini et al. (2002) observed that the degranulation response was independent of Fc ϵ 1 stimulation in Fyn–deficient mast cells and that degranulation was dependent on PI3K in wildtype and mutant cell lines. The degranulation response was dependent on a rise in intracellular calcium that was inhibited in Lyn–deficient

mast cells but intact in Fyn-deficient cells. Degranulation proceeded in Lyn $-/-$ cells due to increased activation and constitutive phosphorylation of the calcium-independent protein kinase C delta isoform (PRKCD; 176977). Paravicini et al. (2002) concluded that Fyn- and Lyn-initiated pathways synergize in late events at the level of protein kinase C and calcium, respectively, to regulate mast cell degranulation. Animal model experiments lend further support to the function of LYN. Hibbs et al. (1995) demonstrated that mice homozygous for a disruption of the Lyn locus display abnormalities associated with the B-lymphocyte lineage and in mast cell function. Despite reduced numbers of recirculating B lymphocytes, the homozygous deficient mice are immunoglobulin M hyperglobulinemic. Lyn-deficient mice show IgM hyperglobulinemia. Immune responses to T-independent and T-dependent antigens were affected. The deficient mice failed to mediate an allergic response to IgE cross-linking, indicating that activation of Lyn plays an indispensable role in signaling by the high-affinity IgE receptor (FCER). Homozygous deficient mice had circulating autoreactive antibodies, and many showed severe glomerulonephritis caused by the deposition of IgG immune complexes in the

kidney, a pathology reminiscent of systemic lupus erythematosus. Hibbs et al. (1995) stated that, collectively, these results implicated LYN as having an indispensable role in immunoglobulin-mediated signaling, particularly in establishing B cell tolerance. Harder et al. (2001) generated mice with a gain-of-function Lyn mutation (tyr508 to phe, which they referred to as 'up') analogous to the tyr527-to-phe activating mutation in the mouse Src gene (OMIM Ref. No. 190090) (Webster et al., 1995). Even aging mice with the Lyn up/up phenotype did not display hematologic malignancies, unlike Lyn $-/-$ mice, which developed splenomegaly, increased myeloid progenitors, and monocyte/macrophage tumors. Biochemical analysis revealed that Lyn is essential in establishing ITIM (immunoreceptor tyrosine-based inhibitory motif)-dependent signaling and for the activation of specific protein tyrosine phosphatases within myeloid cells, which may underlie the susceptibility of Lyn $-/-$ mice to tumorigenesis. Hasegawa et al. (2001) generated mice deficient in both Cd19 (OMIM Ref. No. 107265) and Lyn. Cd19 deficiency

[14765] It is appreciated that the abovementioned animal model for LYN is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14766] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14767] Harder, K. W.; Parsons, L. M.; Armes, J.; Evans, N.; Kountouri, N.; Clark, R.; Quillici, C.; Grail, D.; Hodgson, G. S.; Dunn, A. R.; Hibbs, M. L. : Gain- and loss-of-function Lyn mutant mice define a critical inhibitory role for Lyn in the myeloid lineage. *Immunity* 15: 603–615, 2001. ; and

[14768] Parravicini, V.; Gadina, M.; Kovarova, M.; Odom, S.; Gonzalez-Espinosa, C.; Furumoto, Y.; Saitoh, S.; Samelson, L. E.; O'Shea, J. J.; Rivera, J. : Fyn kinase initiates complementary signal.

[14769] Further studies establishing the function and utilities of LYN are found in John Hopkins OMIM database record ID 165120, and in cited publications numbered 2976, 4818, 510 and 5110–5111 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926) is another VGAM247 host target gene. MBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

MBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MBD3 BINDING SITE, designated SEQ ID:10022, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14770] Another function of VGAM247 is therefore inhibition of Methyl-CpG Binding Domain Protein 3 (MBD3, Accession NM_003926), a gene which are subunits of the NURD (nucleosome remodeling and histone deacetylase) complex . Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MBD3. The function of MBD3 has been established by previous studies. The MECP2 (OMIM Ref. No. 300005) and MBD1 (OMIM Ref. No. 156535) proteins bind specifically to methylated DNA via a methyl-CpG-binding domain (MBD). Both proteins can repress transcription and appear to be important in interpreting the signal that methylation of DNA represents. By searching an EST database for proteins containing an MBD-like motif, Hendrich and Bird (1998) identified human and mouse cDNAs encoding the 3 novel proteins MBD2 (OMIM Ref. No. 603547), MBD3, and MBD4 (OMIM Ref. No.

603574). The predicted 291–amino acid human MBD3 protein (GenBank AF072247) is 94% identical to mouse Mbd3. MBD3 failed to specifically bind methylated DNA in vitro. A green fluorescence protein (GFP)–MBD3 fusion protein showed diffuse nuclear staining in cells in which it was expressed at low levels, and accumulated in many nuclear foci in cells in which it was expressed at high levels. However, MBD3 did not appear to associate with the highly methylated major satellite DNA in mouse cells. The authors identified cDNAs representing an alternatively spliced mouse Mbd3 mRNA that lacks the coding sequence for the N–terminal half of the MBD. RT–PCR analysis of many mouse tissues indicated that this shorter message constitutes a significant fraction of total Mbd3 transcripts. Northern blot analysis detected Mbd3 transcripts in all mouse tissues tested. Zhang et al. (1999) showed that MTA2 (MTA1L1; 603947) and the 32–kD MBD3 protein are subunits of the NURD (nucleosome remodeling and histone deacetylase) complex (see OMIM Ref. No. MTA1; 603526). Immunoprecipitation analysis showed that MBD3 interacts with HDAC1 (OMIM Ref. No. 601241), RBBP4 (OMIM Ref. No. 602923), and RBBP7 (OMIM Ref. No. 602922), but not with MI2 (CHD4;

603277), suggesting that MBD3 is embedded within the NURD complex. The authors found that MTA2 directs the assembly of an active histone deacetylase complex and that the association of MTA2 with the complex requires MBD3. Gel mobility shift analysis determined that both NURD and MBD3 are unable to bind to methylated DNA in the absence of MBD2. Zhang et al. (1999) proposed that NURD is involved in the transcriptional repression of methylated DNA. Wade et al. (1999) also identified MTA1, MTA1L, and MBD3 as components of the NURD complex, which they referred to as the MI2 complex.

[14771] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14772] Zhang, Y.; Ng, H.-H.; Erdjument-Bromage, H; Tempst, P.; Bird, A.; Reinberg, D. : Analysis of the NuRD subunits reveals a histone deacetylase core complex and a connection with DNA methylation. *Genes Dev.* 13: 1924–1935, 1999. ; and

[14773] Hendrich, B.; Bird, A. : Identification and characterization of a family of mammalian methyl-CpG binding proteins. *Molec. Cell. Biol.* 18: 6538–6547, 1998.

[14774] Further studies establishing the function and utilities of

MBD3 are found in John Hopkins OMIM database record ID 603573, and in cited publications numbered 2226, 5359–5360, 506 and 5361 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_139202) is another VGAM247 host target gene. MLC1 BINDING SITE1 and MLC1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MLC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLC1 BINDING SITE1 and MLC1 BINDING SITE2, designated SEQ ID:29220 and SEQ ID:17526 respectively, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14775] Another function of VGAM247 is therefore inhibition of Megalencephalic Leukoencephalopathy with Subcortical Cysts 1 (MLC1, Accession NM_139202). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLC1. Sialidase 3 (membrane sialidase) (NEU3, Accession NM_006656) is another VGAM247 host target gene. NEU3

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEU3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEU3 BINDING SITE, designated SEQ ID:13455, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14776] Another function of VGAM247 is therefore inhibition of Sialidase 3 (membrane sialidase) (NEU3, Accession NM_006656). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEU3. Podocalyxin-like (PODXL, Accession NM_005397) is another VGAM247 host target gene. PODXL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PODXL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PODXL BINDING SITE, designated SEQ ID:11876, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14777] Another function of VGAM247 is therefore inhibition of Podocalyxin-like (PODXL, Accession NM_005397), a gene which is an antiadhesin. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PODXL. The function of PODXL has been established by previous studies. The renal glomerular epithelial cell, or podocyte, is a highly differentiated cell with characteristic interdigitating foot processes covering the outer aspect of the glomerular basement membrane. The foot processes are covered on their apical surface with a polyanionic glycocalyx, which is an essential element of the glomerular filter. Podocalyxin, a sialoglycoprotein, is thought to be a major component of this glycocalyx. By screening human renal cortex and heart cDNA libraries with a rabbit podocalyxin-like protein-1 (PCLP1) cDNA, Kershaw et al. (1997) cloned cDNAs encoding human PCLP, or PODXL. Northern blot analysis revealed that PODXL is expressed as a major 5.9-kb transcript and minor 4.4- and 9.6-kb transcripts in various tissues, with highest expression in kidney, pancreas, and heart. The predicted 528-amino acid protein has a 21-amino acid signal peptide, a transmembrane domain, and a highly acidic intracellular domain. The amino

acid sequence of human PODXL is 48% identical to that of rabbit PCLP1, with 96% identity in the transmembrane and intracellular domains. The calculated molecular mass of PODXL is 54 kD. Western blot analysis of renal glomerular extracts showed that monoclonal antibodies against human PODXL recognize a 160/165-kD human PODXL doublet, rat podocalyxin, and rabbit PCLP1. Kershaw et al. (1997) suggested that the discrepancy between the calculated and observed masses of human PODXL is due to posttranslational modifications. By immunofluorescence of human kidney sections using antibodies against PODXL, Kershaw et al. (1997) found intense vascular endothelial cell and glomerular staining. Kershaw et al. (1997) mapped the human PODXL gene to 7q32-q33 by fluorescence in situ hybridization.

[14778] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14779] Kershaw, D. B.; Beck, S. G.; Wharram, B. L.; Wiggins, J. E.; Goyal, M.; Thomas, P. E.; Wiggins, R. C. : Molecular cloning and characterization of human podocalyxin-like protein: orthologous relationship to rabbit PCLP1 and rat podocalyxin. J. Biol. Chem. 272: 15708-15714, 1997. ;

and

[14780] Kershaw, D. B.; Wiggins, J. E.; Wharram, B. L.; Wiggins, R. C. : Assignment of the human podocalyxin-like protein (PODXL) gene to 7q32-q33. Genomics 45: 239-240, 1997.

[14781] Further studies establishing the function and utilities of PODXL are found in John Hopkins OMIM database record ID 602632, and in cited publications numbered 8749-8750 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 2 (facilitated glucose transporter), Member 3 (SLC2A3, Accession NM_006931) is another VGAM247 host target gene. SLC2A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A3 BINDING SITE, designated SEQ ID:13817, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14782] Another function of VGAM247 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter),

Member 3 (SLC2A3, Accession NM_006931), a gene which probably is a neuronal glucose transporter. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A3. The function of SLC2A3 has been established by previous studies. Gould and Holman (1993), who provided a review of the glucose transporter family, referred to GLUT3 as the brain-type glucose transporter. It appears that high GLUT3 protein expression is confined generally to tissues that exhibit a high glucose demand, such as brain and nerve. Hauguel-de Mouzon et al. (1997) examined the cellular localization of GLUT3 mRNA and protein. In situ hybridization showed that GLUT3 mRNA was present in the trophoblast cell layer and in vascular endothelium with a heterogeneous distribution pattern. GLUT3 protein, migrating at an apparent molecular mass of 49 kD, was detected by immunoblotting in membranes from whole placenta and endothelial cells derived from intraplacental microvessels, but not in isolated trophoblast cells. This cell-specific pattern of expression was confirmed by immunocytochemical studies showing localization of GLUT3 protein in vascular endothelium. Based on the cell-specific distribution of GLUT3 protein at the

fetal interface, the authors suggested that this protein may be important in the transport of glucose from the placenta to the fetal circulation.

[14783] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14784] Gould, G. W.; Holman, G. D. : The glucose transporter family: structure, function and tissue-specific expression. *Biochem. J.* 295: 329–341, 1993. ; and

[14785] Hauguel-de Mouzon, S.; Challier, J. C.; Kacemi, A.; Cauzac, M.; Malek, A.; Girard, J. : The GLUT3 glucose transporter isoform is differentially expressed within human placental cell types.

[14786] Further studies establishing the function and utilities of SLC2A3 are found in John Hopkins OMIM database record ID 138170, and in cited publications numbered 11908–11912 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transcription Elongation Factor A (SII), 1 (TCEA1, Accession XM_087370) is another VGAM247 host target gene. TCEA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCEA1, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCEA1 BINDING SITE, designated SEQ ID:39203, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14787] Another function of VGAM247 is therefore inhibition of Transcription Elongation Factor A (SII), 1 (TCEA1, Accession XM_087370), a gene which helps RNA polymerase II to transcribe past blockages. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCEA1. The function of TCEA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM211.TIC (Accession NM_012455) is another VGAM247 host target gene. TIC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TIC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIC BINDING SITE, designated SEQ ID:14829, to the nucleotide sequence of

VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14788] Another function of VGAM247 is therefore inhibition of TIC (Accession NM_012455). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIC. TSG (Accession NM_020648) is another VGAM247 host target gene. TSG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TSG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TSG BINDING SITE, designated SEQ ID:21812, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14789] Another function of VGAM247 is therefore inhibition of TSG (Accession NM_020648). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TSG. Thioredoxin Reductase 1 (TXNRD1, Accession NM_003330) is another VGAM247 host target gene. TXNRD1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

TXNRD1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TXNRD1 BINDING SITE, designated SEQ ID:9336, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14790] Another function of VGAM247 is therefore inhibition of Thioredoxin Reductase 1 (TXNRD1, Accession NM_003330), a gene which acts as an antioxidant enzyme and is involved in maintaining redox balance. Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TXNRD1. The function of TXNRD1 has been established by previous studies. Thioredoxin reductase (EC 1.6.4.5) is a key enzyme in the regulation of the intracellular redox environment. Gasdaska et al. (1995) purified human thioredoxin reductase from placenta and obtained amino acid sequence from tryptic peptides. Based on protein sequence data, the authors designed degenerate PCR primers and used them to screen a human placental cDNA library. The authors obtained a 3.8-kb cDNA encoding a predicted 495-amino acid protein that is 40% identical to

glutathione reductase and 24% identical to thioredoxin reductase from *E. coli*. The protein is predicted to contain a FAD-binding domain, as expected, but this activity could not be demonstrated with recombinantly expressed enzyme. By Northern blot analysis, Gasdaska et al. (1996) found that thioredoxin reductase was expressed in all tissues examined but at varying levels. The authors found no correlation between the relative expression levels of thioredoxin and thioredoxin reductase. See also selenocysteine-containing thioredoxin reductase (OMIM Ref. No. 601339). Selenium has been indirectly implicated in immunologic function and numerous nutritional studies over many years. Furthermore, HIV-infected persons are reported to have decreased levels of plasma selenium and selenium-containing glutathione peroxidase (e.g., 138321). For this reason, Gladyshev et al. (1996) initiated studies on selenium metabolism in human T cells. The authors identified one of the selenoproteins detected in T cells as thioredoxin reductase and demonstrated that the location of selenocysteine in this protein corresponds to a TGA codon in the cloned placental gene. The finding that T-cell thioredoxin reductase is a selenoenzyme that contains selenium in a conserved C-terminal region provides

another example of the role of selenium in the major antioxidant enzyme system (i.e., thioredoxin–thioredoxin reductase), in addition to the well-known glutathione peroxidase enzyme system.

[14791] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14792] Gasdaska, J. R.; Gasdaska, P. Y.; Gallegos, A.; Powis, G. : Human thioredoxin reductase gene localization to chromosomal position 12q23–q24.1 and mRNA distribution in human tissue. *Genomics* 37: 257–259, 1996. ; and

[14793] Gasdaska, P. Y.; Gasdaska, J. R.; Cochran, S.; Powis, G. : Cloning and sequencing of a human thioredoxin reductase. *FEBS Lett.* 373: 5–9, 1995.

[14794] Further studies establishing the function and utilities of TXNRD1 are found in John Hopkins OMIM database record ID 601112, and in cited publications numbered 10041–1004 and 9635 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A2BP1 (Accession NM_018723) is another VGAM247 host target gene. A2BP1 BINDING SITE1 and A2BP1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by A2BP1, corre–

sponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of A2BP1 BINDING SITE1 and A2BP1 BINDING SITE2, designated SEQ ID:20807 and SEQ ID:20808 respectively, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14795] Another function of VGAM247 is therefore inhibition of A2BP1 (Accession NM_018723). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with A2BP1. Ras Homolog Gene Family, Member U (ARHU, Accession NM_021205) is another VGAM247 host target gene. ARHU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHU BINDING SITE, designated SEQ ID:22184, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14796] Another function of VGAM247 is therefore inhibition of Ras Homolog Gene Family, Member U (ARHU, Accession

NM_021205). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHU. DKFZp547I094 (Accession NM_032155) is another VGAM247 host target gene. DKFZp547I094 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp547I094, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547I094 BINDING SITE, designated SEQ ID:25857, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14797] Another function of VGAM247 is therefore inhibition of DKFZp547I094 (Accession NM_032155). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547I094. Double C2-like Domains, Beta (DOC2B, Accession NM_003585) is another VGAM247 host target gene. DOC2B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DOC2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DOC2B BINDING SITE, designated SEQ ID:9638, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14798] Another function of VGAM247 is therefore inhibition of Double C2-like Domains, Beta (DOC2B, Accession NM_003585). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DOC2B. FASTK (Accession NM_025096) is another VGAM247 host target gene. FASTK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FASTK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FASTK BINDING SITE, designated SEQ ID:24730, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14799] Another function of VGAM247 is therefore inhibition of FASTK (Accession NM_025096). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FASTK.

FLJ12975 (Accession XM_045522) is another VGAM247 host target gene. FLJ12975 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12975, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12975 BINDING SITE, designated SEQ ID:34480, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14800] Another function of VGAM247 is therefore inhibition of FLJ12975 (Accession XM_045522). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12975. FLJ14297 (Accession NM_024903) is another VGAM247 host target gene. FLJ14297 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14297, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14297 BINDING SITE, designated SEQ ID:24391, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2958.

[14801] Another function of VGAM247 is therefore inhibition of FLJ14297 (Accession NM_024903). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14297. FLJ21687 (Accession NM_024859) is another VGAM247 host target gene. FLJ21687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21687 BINDING SITE, designated SEQ ID:24290, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14802] Another function of VGAM247 is therefore inhibition of FLJ21687 (Accession NM_024859). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21687. FLJ22559 (Accession NM_024928) is another VGAM247 host target gene. FLJ22559 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ22559, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22559 BINDING SITE, designated SEQ ID:24465, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14803] Another function of VGAM247 is therefore inhibition of FLJ22559 (Accession NM_024928). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22559. FLJ23071 (Accession NM_025192) is another VGAM247 host target gene. FLJ23071 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23071 BINDING SITE, designated SEQ ID:24847, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14804] Another function of VGAM247 is therefore inhibition of FLJ23071 (Accession NM_025192). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ23071. FLJ23168 (Accession NM_025055) is another VGAM247 host target gene. FLJ23168 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23168, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23168 BINDING SITE, designated SEQ ID:24652, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14805] Another function of VGAM247 is therefore inhibition of FLJ23168 (Accession NM_025055). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23168. jdp2 (Accession NM_130469) is another VGAM247 host target gene. jdp2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by jdp2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of jdp2 BINDING SITE, designated SEQ ID:28230, to the nucleotide sequence of VGAM247 RNA,

herein designated VGAM RNA, also designated SEQ ID:2958.

[14806] Another function of VGAM247 is therefore inhibition of jdp2 (Accession NM_130469). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with jdp2. KIAA0557 (Accession XM_085507) is another VGAM247 host target gene. KIAA0557 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0557, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0557 BINDING SITE, designated SEQ ID:38207, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14807] Another function of VGAM247 is therefore inhibition of KIAA0557 (Accession XM_085507). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0557. KIAA0599 (Accession XM_085127) is another VGAM247 host target gene. KIAA0599 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by KIAA0599, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0599 BINDING SITE, designated SEQ ID:37857, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14808] Another function of VGAM247 is therefore inhibition of KIAA0599 (Accession XM_085127). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0599. KIAA0674 (Accession XM_027054) is another VGAM247 host target gene. KIAA0674 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0674, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0674 BINDING SITE, designated SEQ ID:30400, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14809] Another function of VGAM247 is therefore inhibition of KIAA0674 (Accession XM_027054). Accordingly, utilities

of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0674. KIAA1340 (Accession XM_044836) is another VGAM247 host target gene. KIAA1340 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1340 BINDING SITE, designated SEQ ID:34296, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14810] Another function of VGAM247 is therefore inhibition of KIAA1340 (Accession XM_044836). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1340. KIAA1465 (Accession XM_027396) is another VGAM247 host target gene. KIAA1465 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1465, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1465 BINDING SITE, designated SEQ ID:30505, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14811] Another function of VGAM247 is therefore inhibition of KIAA1465 (Accession XM_027396). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1465. KIAA1649 (Accession NM_032311) is another VGAM247 host target gene. KIAA1649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1649 BINDING SITE, designated SEQ ID:26109, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14812] Another function of VGAM247 is therefore inhibition of KIAA1649 (Accession NM_032311). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1649. KIAA1918 (Accession XM_054951) is another VGAM247 host target gene. KIAA1918 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1918 BINDING SITE, designated SEQ ID:36215, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14813] Another function of VGAM247 is therefore inhibition of KIAA1918 (Accession XM_054951). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1918. MGC11349 (Accession NM_025112) is another VGAM247 host target gene. MGC11349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC11349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11349 BINDING SITE, designated SEQ ID:24760, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14814] Another function of VGAM247 is therefore inhibition of

MGC11349 (Accession NM_025112). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11349. MGC2821 (Accession NM_024054) is another VGAM247 host target gene. MGC2821 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC2821, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2821 BINDING SITE, designated SEQ ID:23489, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14815] Another function of VGAM247 is therefore inhibition of MGC2821 (Accession NM_024054). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2821. MGC35558 (Accession NM_145013) is another VGAM247 host target gene. MGC35558 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC35558, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC35558 BINDING SITE, designated SEQ ID:29614, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14816] Another function of VGAM247 is therefore inhibition of MGC35558 (Accession NM_145013). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC35558. MGC4368 (Accession NM_024510) is another VGAM247 host target gene. MGC4368 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC4368, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4368 BINDING SITE, designated SEQ ID:23700, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14817] Another function of VGAM247 is therefore inhibition of MGC4368 (Accession NM_024510). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4368. MGC7036 (Accession NM_145058) is another

VGAM247 host target gene. MGC7036 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC7036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC7036 BINDING SITE, designated SEQ ID:29694, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14818] Another function of VGAM247 is therefore inhibition of MGC7036 (Accession NM_145058). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC7036. Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM_167803) is another VGAM247 host target gene. PCANAP7 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PCANAP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PCANAP7 BINDING SITE, designated SEQ ID:44838, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2958.

[14819] Another function of VGAM247 is therefore inhibition of Prostate Cancer Associated Protein 7 (PCANAP7, Accession XM_167803). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PCANAP7. Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM_138687) is another VGAM247 host target gene. PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PIP5K2B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K2B BINDING SITE1 and PIP5K2B BINDING SITE2, designated SEQ ID:28930 and SEQ ID:9614 respectively, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14820] Another function of VGAM247 is therefore inhibition of Phosphatidylinositol-4-phosphate 5-kinase, Type II, Beta (PIP5K2B, Accession NM_138687). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K2B.

SNF1 Sucrose Nonfermenting Like Kinase (yeast) (SLK, Accession NM_014720) is another VGAM247 host target gene. SLK BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLK BINDING SITE, designated SEQ ID:16281, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14821] Another function of VGAM247 is therefore inhibition of SNF1 Sucrose Nonfermenting Like Kinase (yeast) (SLK, Accession NM_014720). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLK. ZFP106 (Accession NM_022473) is another VGAM247 host target gene. ZFP106 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP106, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP106 BINDING SITE, designated SEQ ID:22833, to the nucleotide sequence of VGAM247 RNA,

herein designated VGAM RNA, also designated SEQ ID:2958.

[14822] Another function of VGAM247 is therefore inhibition of ZFP106 (Accession NM_022473). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP106. LOC130617 (Accession NM_138802) is another VGAM247 host target gene. LOC130617 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC130617, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130617 BINDING SITE, designated SEQ ID:29025, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14823] Another function of VGAM247 is therefore inhibition of LOC130617 (Accession NM_138802). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130617. LOC132332 (Accession XM_072306) is another VGAM247 host target gene. LOC132332 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC132332, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC132332 BINDING SITE, designated SEQ ID:37488, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14824] Another function of VGAM247 is therefore inhibition of LOC132332 (Accession XM_072306). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC132332. LOC144195 (Accession XM_016498) is another VGAM247 host target gene. LOC144195 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144195, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144195 BINDING SITE, designated SEQ ID:30265, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14825] Another function of VGAM247 is therefore inhibition of LOC144195 (Accession XM_016498). Accordingly, utilities

of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144195. LOC144893 (Accession XM_096687) is another VGAM247 host target gene. LOC144893 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC144893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144893 BINDING SITE, designated SEQ ID:40461, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14826] Another function of VGAM247 is therefore inhibition of LOC144893 (Accession XM_096687). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144893. LOC146375 (Accession XM_085434) is another VGAM247 host target gene. LOC146375 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC146375, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC146375 BINDING SITE, designated SEQ ID:38141, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14827] Another function of VGAM247 is therefore inhibition of LOC146375 (Accession XM_085434). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146375. LOC157543 (Accession XM_088325) is another VGAM247 host target gene. LOC157543 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157543, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157543 BINDING SITE, designated SEQ ID:39611, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14828] Another function of VGAM247 is therefore inhibition of LOC157543 (Accession XM_088325). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157543. LOC201294 (Accession XM_113950) is another VGAM247 host target gene. LOC201294 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201294, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201294 BINDING SITE, designated SEQ ID:42568, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14829] Another function of VGAM247 is therefore inhibition of LOC201294 (Accession XM_113950). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201294. LOC202181 (Accession XM_114456) is another VGAM247 host target gene. LOC202181 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC202181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202181 BINDING SITE, designated SEQ ID:42969, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14830] Another function of VGAM247 is therefore inhibition of

LOC202181 (Accession XM_114456). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC202181. LOC203084 (Accession XM_113540) is another VGAM247 host target gene. LOC203084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203084 BINDING SITE, designated SEQ ID:42281, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14831] Another function of VGAM247 is therefore inhibition of LOC203084 (Accession XM_113540). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203084. LOC203427 (Accession XM_114699) is another VGAM247 host target gene. LOC203427 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC203427, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC203427 BINDING SITE, designated SEQ ID:43045, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14832] Another function of VGAM247 is therefore inhibition of LOC203427 (Accession XM_114699). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203427. LOC219855 (Accession XM_166184) is another VGAM247 host target gene. LOC219855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219855 BINDING SITE, designated SEQ ID:43997, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14833] Another function of VGAM247 is therefore inhibition of LOC219855 (Accession XM_166184). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219855. LOC219994 (Accession XM_167792) is an-

other VGAM247 host target gene. LOC219994 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219994, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219994 BINDING SITE, designated SEQ ID:44835, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14834] Another function of VGAM247 is therefore inhibition of LOC219994 (Accession XM_167792). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219994. LOC51103 (Accession XM_031645) is another VGAM247 host target gene. LOC51103 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51103, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51103 BINDING SITE, designated SEQ ID:31446, to the nucleotide sequence of VGAM247 RNA, herein designated VGAM RNA, also designated SEQ ID:2958.

[14835] Another function of VGAM247 is therefore inhibition of LOC51103 (Accession XM_031645). Accordingly, utilities of VGAM247 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51103. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 248 (VGAM248) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14836] VGAM248 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM248 was detected is described hereinabove with reference to Figs. 1–8.

[14837] VGAM248 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14838] VGAM248 gene encodes a VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM248

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM248 precursor RNA is designated SEQ ID:234, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:234 is located at position 106248 relative to the genome of Calitrichine Herpesvirus 3.

[14839] VGAM248 precursor RNA folds onto itself, forming VGAM248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14840] An enzyme complex designated DICER COMPLEX, `dices` the VGAM248 folded precursor RNA into VGAM248 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 53%) nucleotide sequence of VGAM248 RNA is designated SEQ ID:2959, and is provided hereinbelow with reference to the sequence listing part.

[14841] VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM248 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[14842] VGAM248 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM248 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM248 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14843] The complementary binding of VGAM248 RNA, herein designated VGAM RNA, to host target binding sites on VGAM248 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM248 host target RNA into VGAM248 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14844] It is appreciated that VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM248 host target genes. The mRNA of each one of this plurality of VGAM248 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM248 RNA, herein designated VGAM RNA, and which when bound by VGAM248 RNA causes inhibition of translation of respective one or more VGAM248 host target proteins.

[14845] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM248 gene, herein designated VGAM GENE, on one or more VGAM248 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14846] It is yet further appreciated that a function of VGAM248 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM248 correlate with, and may be deduced from, the identity of the host target genes which VGAM248 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14847] Nucleotide sequences of the VGAM248 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM248 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM248 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM248 are further described hereinbelow with reference to Table 1.

[14848] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM248 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM248 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[14849] As mentioned hereinabove with reference to Fig. 1, a function of VGAM248 gene, herein designated VGAM is inhibition of expression of VGAM248 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM248 correlate with, and may be deduced from, the identity of the target genes which VGAM248 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14850] BCLG (Accession NM_030766) is a VGAM248 host target gene. BCLG BINDING SITE1 and BCLG BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by BCLG, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCLG BINDING SITE1 and BCLG BINDING SITE2, designated SEQ ID:25053 and SEQ ID:28967 respectively, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14851] A function of VGAM248 is therefore inhibition of BCLG (Accession NM_030766). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with BCLG. Zinc Finger Protein 42 (myeloid-specific retinoic acid- responsive) (ZNF42, Accession NM_003422) is another VGAM248 host target gene. ZNF42 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZNF42, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF42 BINDING SITE, designated SEQ ID:9468, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14852] Another function of VGAM248 is therefore inhibition of Zinc Finger Protein 42 (myeloid-specific retinoic acid- responsive) (ZNF42, Accession NM_003422), a gene which may be one regulator of transcriptional events during hemopoietic development. Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF42. The function of ZNF42 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.DKFZP434I0714 (Accession XM_098247) is

another VGAM248 host target gene. DKFZP434I0714 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434I0714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434I0714 BINDING SITE, designated SEQ ID:41531, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14853] Another function of VGAM248 is therefore inhibition of DKFZP434I0714 (Accession XM_098247). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434I0714. FLJ14082 (Accession NM_025024) is another VGAM248 host target gene. FLJ14082 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14082 BINDING SITE, designated SEQ ID:24611, to the nucleotide sequence of VGAM248 RNA, herein designated

VGAM RNA, also designated SEQ ID:2959.

[14854] Another function of VGAM248 is therefore inhibition of FLJ14082 (Accession NM_025024). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14082. KIAA0632 (Accession NM_015545) is another VGAM248 host target gene. KIAA0632 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0632, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0632 BINDING SITE, designated SEQ ID:17806, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14855] Another function of VGAM248 is therefore inhibition of KIAA0632 (Accession NM_015545). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0632. KIAA1010 (Accession XM_050742) is another VGAM248 host target gene. KIAA1010 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1010, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1010 BINDING SITE, designated SEQ ID:35669, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14856] Another function of VGAM248 is therefore inhibition of KIAA1010 (Accession XM_050742). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1010. LOC148089 (Accession XM_086040) is another VGAM248 host target gene. LOC148089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148089 BINDING SITE, designated SEQ ID:38449, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14857] Another function of VGAM248 is therefore inhibition of LOC148089 (Accession XM_086040). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC148089. LOC222031 (Accession XM_168371) is another VGAM248 host target gene. LOC222031 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC222031, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222031 BINDING SITE, designated SEQ ID:45130, to the nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14858] Another function of VGAM248 is therefore inhibition of LOC222031 (Accession XM_168371). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222031. LOC93589 (Accession XM_052387) is another VGAM248 host target gene. LOC93589 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC93589, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC93589 BINDING SITE, designated SEQ ID:35980, to the

nucleotide sequence of VGAM248 RNA, herein designated VGAM RNA, also designated SEQ ID:2959.

[14859] Another function of VGAM248 is therefore inhibition of LOC93589 (Accession XM_052387). Accordingly, utilities of VGAM248 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC93589. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 249 (VGAM249) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14860] VGAM249 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM249 was detected is described hereinabove with reference to Figs. 1–8.

[14861] VGAM249 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14862] VGAM249 gene encodes a VGAM249 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM249 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM249 precursor RNA is designated SEQ ID:235, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:235 is located at position 15261 relative to the genome of Calitrichine Herpesvirus 3.

[14863] VGAM249 precursor RNA folds onto itself, forming VGAM249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14864] An enzyme complex designated DICER COMPLEX, `dices` the VGAM249 folded precursor RNA into VGAM249 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM249 RNA is designated SEQ ID:2960, and is provided hereinbelow with reference to the sequence listing part.

[14865] VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM249 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14866] VGAM249 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM249 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM249 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14867] The complementary binding of VGAM249 RNA, herein designated VGAM RNA, to host target binding sites on VGAM249 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM249 host target RNA into VGAM249 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14868] It is appreciated that VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM249 host target genes. The mRNA of each one of this plurality of VGAM249 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM249 RNA, herein designated VGAM RNA, and which when bound by VGAM249 RNA causes inhibition of translation of respective one or more VGAM249 host target proteins.

[14869] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM249 gene, herein designated VGAM GENE, on one or more VGAM249 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[14870] It is yet further appreciated that a function of VGAM249 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM249 correlate with, and may be deduced from, the identity of the host target genes which VGAM249 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14871] Nucleotide sequences of the VGAM249 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM249 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM249 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM249 are further described hereinbelow with reference to Table 1.

[14872] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM249 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM249 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14873] As mentioned hereinabove with reference to Fig. 1, a function of VGAM249 gene, herein designated VGAM is inhibition of expression of VGAM249 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM249 correlate with, and may be deduced from, the identity of the target genes which VGAM249 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14874] Ubiquitin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087) is a VGAM249 host target gene. UBE2G2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UBE2G2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2G2 BINDING SITE, designated SEQ ID:32376, to the nucleotide sequence of VGAM249 RNA, herein designated VGAM RNA, also designated SEQ ID:2960.

[14875] A function of VGAM249 is therefore inhibition of Ubiqui-

tin-conjugating Enzyme E2G 2 (UBC7 homolog, yeast) (UBE2G2, Accession XM_036087), a gene which catalyzes the covalent attachment of ubiquitin to other proteins. Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UBE2G2. The function of UBE2G2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM164. LOC147118 (Accession XM_097200) is another VGAM249 host target gene. LOC147118 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147118, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147118 BINDING SITE, designated SEQ ID:40807, to the nucleotide sequence of VGAM249 RNA, herein designated VGAM RNA, also designated SEQ ID:2960.

[14876] Another function of VGAM249 is therefore inhibition of LOC147118 (Accession XM_097200). Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC147118. LOC148089 (Accession XM_086040) is another VGAM249 host target gene. LOC148089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148089, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148089 BINDING SITE, designated SEQ ID:38452, to the nucleotide sequence of VGAM249 RNA, herein designated VGAM RNA, also designated SEQ ID:2960.

[14877] Another function of VGAM249 is therefore inhibition of LOC148089 (Accession XM_086040). Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148089. LOC220883 (Accession XM_166076) is another VGAM249 host target gene. LOC220883 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220883, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220883 BINDING SITE, designated SEQ ID:43851, to the nucleotide sequence of VGAM249 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2960.

[14878] Another function of VGAM249 is therefore inhibition of LOC220883 (Accession XM_166076). Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220883. LOC51279 (Accession NM_016546) is another VGAM249 host target gene. LOC51279 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51279, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51279 BINDING SITE, designated SEQ ID:18617, to the nucleotide sequence of VGAM249 RNA, herein designated VGAM RNA, also designated SEQ ID:2960.

[14879] Another function of VGAM249 is therefore inhibition of LOC51279 (Accession NM_016546). Accordingly, utilities of VGAM249 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51279. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 250 (VGAM250) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14880] VGAM250 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM250 was detected is described hereinabove with reference to Figs. 1–8.

[14881] VGAM250 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14882] VGAM250 gene encodes a VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM250 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM250 precursor RNA is designated SEQ ID:236, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:236 is located at position 23102 relative to the genome of Callitrichine Herpesvirus 3.

[14883] VGAM250 precursor RNA folds onto itself, forming

VGAM250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14884] An enzyme complex designated DICER COMPLEX, `dices` the VGAM250 folded precursor RNA into VGAM250 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM250 RNA is designated SEQ ID:2961, and is provided hereinbelow with reference to the sequence listing part.

[14885] VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM250 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14886] VGAM250 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM250 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM250 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14887] The complementary binding of VGAM250 RNA, herein designated VGAM RNA, to host target binding sites on VGAM250 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM250 host target RNA into VGAM250 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14888] It is appreciated that VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM250 host target genes. The mRNA of each one of this plurality of VGAM250 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM250 RNA, herein designated VGAM RNA, and which when bound by VGAM250 RNA causes inhibition of translation of respective one or more VGAM250 host target proteins.

[14889] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM250 gene, herein designated VGAM GENE, on one or more VGAM250 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14890] It is yet further appreciated that a function of VGAM250 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM250 correlate with, and may be deduced from, the identity of the host target genes which VGAM250 binds and inhibits,

and the function of these host target genes, as elaborated hereinbelow.

[14891] Nucleotide sequences of the VGAM250 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM250 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM250 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM250 are further described hereinbelow with reference to Table 1.

[14892] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM250 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM250 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14893] As mentioned hereinabove with reference to Fig. 1, a function of VGAM250 gene, herein designated VGAM is inhibition of expression of VGAM250 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM250 correlate with, and may be deduced from, the identity of the target genes which VGAM250 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[14894] Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Accession NM_025136) is a VGAM250 host target gene. OPA3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OPA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA3 BINDING SITE, designated SEQ ID:24774, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14895] A function of VGAM250 is therefore inhibition of Optic Atrophy 3 (autosomal recessive, with chorea and spastic paraplegia) (OPA3, Accession NM_025136). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA3. Secreted Frizzled-related Protein 1 (SFRP1, Accession NM_003012) is another VGAM250 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BINDING SITE, designated SEQ ID:8931, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14896] Another function of VGAM250 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 has been established by previous studies. A frequent epigenetic change in cancer involves aberrantly hypermethylated CpG islands in gene promoters, with loss of transcription of the genes (Baylin and Herman, (2000)) Cameron et al. (1999) showed that silencing of hypermethylated genes in cancer is dependent on both methylation of dense CpG islands and histone deacetylase (see OMIM Ref. No. 601241) activity. Suzuki et al. (2002) used cDNA microarray analysis to screen for genes that are epigenetically silenced in human colorectal cancer. By screening over 10,000 genes, they showed that they could identify a substantial number of

genes with promoter hypermethylation in a given cancer; these are distinct from genes with unmethylated promoters, for which increased expression is produced by histone deacetylase inhibition alone. Many of the hypermethylated genes identified have high potential for roles in tumorigenesis by virtue of their predicted function and chromosome position. They also identified a group of genes that are preferentially hypermethylated in colorectal cancer and gastric cancer. One of these genes, SFRP1, belongs to a gene family; Suzuki et al. (2002) showed that hypermethylation of 4 genes in this family occur frequently in colorectal cancer, providing for (i) a unique potential mechanism for loss of tumor suppressor gene function and (ii) construction of a molecular marker panel that could detect virtually all colorectal cancer. Fukuhara et al. (2002) investigated the expression and function of SFRP1 in uterine leiomyomas. Northern and Western blot analyses detected increased SFRP1 expression in leiomyomas compared with normal myometrium. Expression was strongest in the late follicular phase (high estrogenic milieu) of the menstrual cycle. Interestingly, expression was negligible in leiomyomas treated with GNRH agonist. The authors concluded that strong SFRP1 expression, which

appeared to be independent of cell proliferation, under high estrogenic conditions contributes to the development of uterine leiomyomas through the antiapoptotic effect of SFRP1.

[14897] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14898] Suzuki, H.; Gabrielson, E.; Chen, W.; Anbazhagan, R.; van Engeland, M.; Weijenberg, M. P.; Herman, J. G.; Baylin, S. B. : A genomic screen for genes upregulated by demethylation and histone deacetylase inhibition in human colorectal cancer. *Nature Genet.* 31: 141–149, 2002. ; and

[14899] Fukuhara, K.; Kariya, M.; Kita, M.; Shime, H.; Kanamori, T.; Kosaka, C.; Orii, A.; Fujita, J.; Fujii, S. : Secreted frizzled related protein 1 is overexpressed in uterine leiomyomas, *ass.*

[14900] Further studies establishing the function and utilities of SFRP1 are found in John Hopkins OMIM database record ID 604156, and in cited publications numbered 420–425 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM_000351) is another VGAM250 host target gene. STS

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STS BINDING SITE, designated SEQ ID:5909, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14901] Another function of VGAM250 is therefore inhibition of Steroid Sulfatase (microsomal), Arylsulfatase C, Isozyme S (STS, Accession NM_000351). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STS. TNF Receptor-associated Factor 1 (TRAF1, Accession NM_005658) is another VGAM250 host target gene. TRAF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRAF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRAF1 BINDING SITE, designated SEQ ID:12199, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ

ID:2961.

[14902] Another function of VGAM250 is therefore inhibition of TNF Receptor-associated Factor 1 (TRAF1, Accession NM_005658), a gene which signal transducer associated with the cytoplasmic domain of the 75 kda tumor necrosis factor receptor (tnf-r2). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRAF1. The function of TRAF1 has been established by previous studies. In order to determine how tumor necrosis factor (TNF; 191160) elicits cellular response, factors that interact with the cytoplasmic domain of TNF receptor-2 (TNFR2; 191191) were identified. Rothe et al. (1994) used the yeast-based 2-hybrid system to detect mouse proteins that interact with TNFR2. They identified and cloned 2 TNF receptor-associated factors, which they termed TRAF1 and TRAF2 (OMIM Ref. No. 601895). Each of the TRAFs contains a C-terminal TRAF domain of approximately 230 amino acids. TRAF1 and TRAF2 can form both homo- and heterodimers. Mosialos et al. (1995) identified the human homolog of TRAF1 as Epstein-Barr virus (EBV)-induced mRNA 6 (EBI6), an mRNA that is more abundant in EBV-infected B lymphoblasts than in uninfected control cells.

The predicted 416-amino acid human protein is 86% identical to mouse TRAF1. Both the human and mouse proteins contain N-terminal zinc finger motifs and C-terminal TRAF domains. Northern blot analysis revealed that the 2.6-kb EBI6 mRNA is expressed in lung, spleen, tonsil, and weakly in placenta. Mosialos et al. (1995) found that LMP1, the EBV-transforming protein, specifically associates with LAP1 (TRAF3) or EBI6 in B lymphoblasts. LMP1 expression redirects LAP1 and EBI6 from scattered cytoplasmic structures to LMP1 plasma membrane patches. Both LAP1 and EBI6 associated with the cytoplasmic domain of p80/TNFR2 in vivo. The authors stated that the interaction of LMP1 with the LAP1 and EBI6 TNFR-associated proteins is evidence for the role of these proteins in signaling, and links LMP1-mediated transformation to signal transduction from the TNFR family. The structural hallmark of signal-transducing proteins associated with members of the TNFR superfamily is a novel C-terminal homology region of 230 amino acids, designated the TRAF domain. This domain is involved in a variety of specific protein-protein interactions. Siemienski et al. (1997) found that the human TRAF1 gene has a total length of approximately 12 kb. It is split into 6 exons, 4

of which encode parts of the TRAF domain. Analysis of the genomic structure of the TRAF domains of TRAF2 and TRAF3 (OMIM Ref. No. 601896) suggest that these domains are also encoded by several exons. Animal model experiments lend further support to the function of TRAF1. Tsitsikov et al. (2001) generated Traf1 null mice. Although lymphocyte development was normal, T cells responded to anti-CD3 stimulation with enhanced proliferation. Through TNFR2, but not through TNFR1 (OMIM Ref. No. 191190), they also exhibited enhanced proliferation as well as NFkB (OMIM Ref. No. 164011) and AP1 activation. TNF-induced, lymphocyte-dependent skin necrosis occurred in Traf1 -/- mice at a suboptimal dose of the cytokine. Tsitsikov et al. (2001) concluded that TRAF1 negatively regulates TNFR2-mediated proliferation and NFkB activation

[14903] It is appreciated that the abovementioned animal model for TRAF1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[14904] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [14905] Siemienski, K.; Peters, N.; Scheurich, P.; Wajant, H. : Organization of the human tumour necrosis factor receptor-associated factor 1 (TRAF1) gene and mapping to chromosome 9q33-34. *Gene* 195: 35-39, 1997. ; and
- [14906] Tsitsikov, E. N.; Laouini, D.; Dunn, I. F.; Sannikova, T. Y.; Davidson, L.; Alt, F. W.; Geha, R. S. : TRAF1 is a negative regulator of TNF signaling: enhanced TNF signaling in TRAF1-defi.
- [14907] Further studies establishing the function and utilities of TRAF1 are found in John Hopkins OMIM database record ID 601711, and in cited publications numbered 8862-8865 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA1165 (Accession XM_041162) is another VGAM250 host target gene. KIAA1165 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1165, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1165 BINDING SITE, designated SEQ ID:33477, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14908] Another function of VGAM250 is therefore inhibition of KIAA1165 (Accession XM_041162). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1165. KIAA1822 (Accession XM_041566) is another VGAM250 host target gene. KIAA1822 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1822, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1822 BINDING SITE, designated SEQ ID:33552, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14909] Another function of VGAM250 is therefore inhibition of KIAA1822 (Accession XM_041566). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1822. PRIC285 (Accession XM_028918) is another VGAM250 host target gene. PRIC285 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PRIC285, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRIC285 BINDING SITE, designated SEQ ID:30804, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14910] Another function of VGAM250 is therefore inhibition of PRIC285 (Accession XM_028918). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRIC285. LOC146714 (Accession XM_097072) is another VGAM250 host target gene. LOC146714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146714 BINDING SITE, designated SEQ ID:40721, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14911] Another function of VGAM250 is therefore inhibition of LOC146714 (Accession XM_097072). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC146714. LOC149832 (Accession XM_097733) is another VGAM250 host target gene. LOC149832 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149832 BINDING SITE, designated SEQ ID:41081, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14912] Another function of VGAM250 is therefore inhibition of LOC149832 (Accession XM_097733). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149832. LOC159110 (Accession XM_088753) is another VGAM250 host target gene. LOC159110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159110 BINDING SITE, designated SEQ ID:39942, to the nucleotide sequence of VGAM250 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2961.

[14913] Another function of VGAM250 is therefore inhibition of LOC159110 (Accession XM_088753). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159110. LOC159116 (Accession XM_088752) is another VGAM250 host target gene. LOC159116 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159116, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159116 BINDING SITE, designated SEQ ID:39940, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14914] Another function of VGAM250 is therefore inhibition of LOC159116 (Accession XM_088752). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159116. LOC199958 (Accession XM_117163) is another VGAM250 host target gene. LOC199958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199958, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199958 BINDING SITE, designated SEQ ID:43264, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14915] Another function of VGAM250 is therefore inhibition of LOC199958 (Accession XM_117163). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199958. LOC205251 (Accession XM_119554) is another VGAM250 host target gene. LOC205251 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC205251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC205251 BINDING SITE, designated SEQ ID:43587, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14916] Another function of VGAM250 is therefore inhibition of LOC205251 (Accession XM_119554). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC205251. LOC220021 (Accession XM_167814) is another VGAM250 host target gene. LOC220021 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220021, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220021 BINDING SITE, designated SEQ ID:44852, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14917] Another function of VGAM250 is therefore inhibition of LOC220021 (Accession XM_167814). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220021. LOC254100 (Accession XM_172851) is another VGAM250 host target gene. LOC254100 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254100, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254100 BINDING SITE, designated SEQ ID:46128, to

the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14918] Another function of VGAM250 is therefore inhibition of LOC254100 (Accession XM_172851). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254100. LOC56920 (Accession NM_020163) is another VGAM250 host target gene. LOC56920 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC56920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56920 BINDING SITE, designated SEQ ID:21382, to the nucleotide sequence of VGAM250 RNA, herein designated VGAM RNA, also designated SEQ ID:2961.

[14919] Another function of VGAM250 is therefore inhibition of LOC56920 (Accession NM_020163). Accordingly, utilities of VGAM250 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56920. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 251 (VGAM251) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14920] VGAM251 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM251 was detected is described hereinabove with reference to Figs. 1–8.

[14921] VGAM251 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14922] VGAM251 gene encodes a VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM251 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM251 precursor RNA is designated SEQ ID:237, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:237 is located at position 21575 relative to the genome of Callitrichine Herpesvirus 3.

[14923] VGAM251 precursor RNA folds onto itself, forming VGAM251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14924] An enzyme complex designated DICER COMPLEX, `dices` the VGAM251 folded precursor RNA into VGAM251 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM251 RNA is designated SEQ ID:2962, and is provided hereinbelow with reference to the sequence listing part.

[14925] VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM251 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM251 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14926] VGAM251 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM251 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM251 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14927] The complementary binding of VGAM251 RNA, herein designated VGAM RNA, to host target binding sites on VGAM251 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM251 host target RNA into VGAM251 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14928] It is appreciated that VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM251 host target genes. The mRNA of each one of this plurality of VGAM251 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM251 RNA, herein designated VGAM RNA, and which when bound by VGAM251 RNA causes inhibition of translation of respective one or more VGAM251 host target proteins.

[14929] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM251 gene, herein designated VGAM GENE, on one or more VGAM251 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14930] It is yet further appreciated that a function of VGAM251 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM251 correlate with, and may be deduced from, the identity of

the host target genes which VGAM251 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14931] Nucleotide sequences of the VGAM251 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM251 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM251 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM251 are further described hereinbelow with reference to Table 1.

[14932] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM251 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM251 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[14933] As mentioned hereinabove with reference to Fig. 1, a function of VGAM251 gene, herein designated VGAM is inhibition of expression of VGAM251 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM251 correlate with, and may be deduced from, the identity of the target genes which VGAM251

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14934] Aldehyde Dehydrogenase 3 Family, Member B2 (ALDH3B2, Accession NM_000695) is a VGAM251 host target gene. ALDH3B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH3B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH3B2 BINDING SITE, designated SEQ ID:6358, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14935] A function of VGAM251 is therefore inhibition of Aldehyde Dehydrogenase 3 Family, Member B2 (ALDH3B2, Accession NM_000695), a gene which may play a role in alcohol detoxitation. Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH3B2. The function of ALDH3B2 has been established by previous studies. See ALDH1 (OMIM Ref. No. 100640). Hsu et al. (1995) and Hsu and Chang (1996) reported the cloning, sequencing and expression of the human ALDH8 gene. Hsu et al. (1997)

determined the structure of the ALDH7 (OMIM Ref. No. 600466) and ALDH8 genes. The ALDH7 gene spans about 20 kb of genomic DNA and contains 9 coding exons. The ALDH8 gene is over 10 kb long and contains at least 10 exons. The ALDH8 gene contains an in-frame stop codon at the seventeenth codon position from the first initiator methionine. The coding region of the ALDH7 gene shows about 86% nucleotide identity with the corresponding region of the ALDH8 gene. The numbers and positions of the introns of the 2 genes are conserved, suggesting that gene duplication is involved in the expansion of the ALDH gene family. The human ALDH7 and ALDH8 genes have a close evolutionary relationship with human ALDH3 (OMIM Ref. No. 100660). The International Radiation Hybrid Mapping Consortium mapped the ALDH8 gene to chromosome 11 (OMIM Ref. No. U37519).

[14936] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14937] Hsu, L. C.; Chang, W.-C. : Sequencing and expression of the human ALDH8 encoding a new member of the aldehyde dehydrogenase family. *Gene* 174: 319-322, 1996. ; and

[14938] Hsu, L. C.; Chang, W.-C.; Lin, S. W.; Yoshida, A. : Cloning and characterization of genes encoding four additional human aldehyde dehydrogenase isozymes. *Adv. Exp. Med. Biol.* 372: 159-1.

[14939] Further studies establishing the function and utilities of ALDH3B2 are found in John Hopkins OMIM database record ID 601917, and in cited publications numbered 9140-914 and 7732 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Enhancer of Zeste Homolog 1 (*Drosophila*) (EZH1, Accession NM_001991) is another VGAM251 host target gene. EZH1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EZH1 BINDING SITE, designated SEQ ID:7715, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14940] Another function of VGAM251 is therefore inhibition of Enhancer of Zeste Homolog 1 (*Drosophila*) (EZH1, Accession NM_001991), a gene which may act in transcriptional regulation and heterochromatin maintenance. Accord-

ingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZH1. The function of EZH1 has been established by previous studies. Transcription mapping efforts within chromosome 17q21 identified a human homolog of the *Drosophila* gene 'enhancer of zeste' E(z). In *Drosophila*, the gene acts as a negative regulator of segment identity genes of the Antennapedia and Bithorax complexes. Abel et al. (1996) reported the full-length protein coding sequence of the human homolog, EZH1, and compared the respective protein sequences in human and *Drosophila*. EZH1 encodes a protein of 747 amino acids that displays 55% amino acid identity overall (70% similarity) with the *Drosophila* protein. The strong sequence conservation suggested potential roles for EZH1 in human development as a transcriptional regulator and as a component of protein complexes that stably maintain heterochromatin. EZH1 is expressed as 2 major transcripts in all adult and fetal human tissues surveyed; comparison of cloned cDNAs suggested that alternative splicing may account for at least part of the transcript size differences. Analysis of an EZH1 cDNA revealed an unusual splicing event involving EZH1 and a tandemly linked gene

GPR2 (OMIM Ref. No. 600240) and suggested a potential mechanism for modifying the EZH1 protein in the conserved C-terminal domain. The GPR2 gene maps to 17q21.1–q21.3 in the vicinity of the BRCA1 gene (OMIM Ref. No. 113705). See also EZH2 (OMIM Ref. No. 601573). By FISH, Laible et al. (1999) mapped the mouse Ezh1 gene to chromosome 11.

[14941] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14942] Abel, K. J.; Brody, L. C.; Valdes, J. M.; Erdos, M. R.; McKinley, D. R.; Castilla, L. H.; Merajver, S. D.; Couch, F. J.; Friedman, L. S.; Ostermeyer, E. A.; Lynch, E. D.; King, M.-C.; Welcsh, P. L.; Osborne-Lawrence, S.; Spillman, M.; Bowcock, A. M.; Collins, F. S.; Weber, B. L. : Characterization of EZH1, a human homolog of Drosophila enhancer of zeste near BRCA1. Genomics 37: 161–171, 1996. ; and

[14943] Laible, G.; Haynes, A. R.; Lebersorger, A.; O'Carroll, D.; Mattei, M.-G.; Denny, P.; Brown, S. D. M.; Jenuwein, T. : The murine polycomb-group genes Ezh1 and Ezh2 map close to Hox gene.

[14944] Further studies establishing the function and utilities of EZH1 are found in John Hopkins OMIM database record ID

601674, and in cited publications numbered 9485 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. GATA Binding Protein 2 (GATA2, Accession NM_002050) is another VGAM251 host target gene. GATA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GATA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GATA2 BINDING SITE, designated SEQ ID:7806, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14945] Another function of VGAM251 is therefore inhibition of GATA Binding Protein 2 (GATA2, Accession NM_002050). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GATA2. Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM_005729) is another VGAM251 host target gene. PPIF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPIF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPIF BINDING SITE, designated SEQ ID:12282, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14946] Another function of VGAM251 is therefore inhibition of Peptidylprolyl Isomerase F (cyclophilin F) (PPIF, Accession NM_005729), a gene which catalyzes the cis to trans isomerization of certain proline imidic peptide bonds in oligopeptides. Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPIF. The function of PPIF has been established by previous studies. Cyclophilins, also referred to as rotamases, catalyze the cis to trans isomerization of certain proline imidic peptide bonds in oligopeptides, which can be the rate limiting step in the folding of proteins. By screening a human cDNA library with a CyP1 (peptidyl-prolyl isomerase) probe, Bergsma et al. (1991) isolated a novel cDNA, PPIF, which encodes a 207-amino acid protein. Northern blot analysis showed that PPIF, which the authors termed CYP3, is expressed as a major 2-kb transcript in Jurkat cells. RNA slot blot analysis revealed expression of PPIF in most cell lines and

types. Western blot analysis of Jurkat cells separated by differential centrifugation suggested that PPIF is predominantly associated with membranes or organelles. Bowles et al. (1999) characterized the genomic structure of the PPIF gene, which contains 6 exons. On the multigene physical map constructed by Deloukas et al. (1998), the PPIF gene was found to be located in the 10q21–q23 region. By screening BAC libraries for the presence of CEPH markers, Bowles et al. (1999) mapped the PPIF gene between D10S201 and D10S1777 at 10q22–q23. Bowles et al. (1999) studied PPIF as a candidate gene for a form of familial dilated cardiomyopathy (CMD1C; 601493) that maps to 10q21–q23, but found no mutation in the gene as a cause of the disorder.

[14947] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14948] Bowles, K. R.; Zintz, C.; Abraham, S. E.; Brandon, L.; Bowles, N. E.; Towbin, J. A. : Genomic characterization of the human peptidyl–prolyl–cis–trans–isomerase, mitochondrial precursor gene: assessment of its role in familial dilated cardiomyopathy. Hum. Genet. 105: 582–586, 1999. ; and

[14949] Deloukas, P.; Schuler, G. D.; Gyapay, G.; Beasley, E. M.; Soderlund, C.; Rodriguez-Tome, P.; Hui, L.; Matise, T. C.; McKusick, K. B.; Beckmann, J. S.; Bentolila, S.; Bihoreau, M.-T.; an.

[14950] Further studies establishing the function and utilities of PPIF are found in John Hopkins OMIM database record ID 604486, and in cited publications numbered 4749-475 and 12054 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFB3, Accession NM_003243) is another VGAM251 host target gene. TGFB3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TGFB3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFB3 BINDING SITE, designated SEQ ID:9251, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14951] Another function of VGAM251 is therefore inhibition of Transforming Growth Factor, Beta Receptor III (betaglycan, 300kDa) (TGFB3, Accession NM_003243), a gene which

involves in capturing and retaining TGF-beta for presentation to the signaling receptors. Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFBR3. The function of TGFBR3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM139. Apolipoprotein L, 2 (APOL2, Accession NM_030882) is another VGAM251 host target gene. APOL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL2 BINDING SITE, designated SEQ ID:25160, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14952] Another function of VGAM251 is therefore inhibition of Apolipoprotein L, 2 (APOL2, Accession NM_030882). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL2. Calneuron 1 (CALN1, Accession

NM_031468) is another VGAM251 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25511, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14953] Another function of VGAM251 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. DKFZP434E2135 (Accession NM_030804) is another VGAM251 host target gene. DKFZP434E2135 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DKFZP434E2135, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434E2135 BINDING SITE, designated SEQ ID:25111, to the nucleotide sequence of

VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14954] Another function of VGAM251 is therefore inhibition of DKFZP434E2135 (Accession NM_030804). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434E2135. DKFZP586F1524 (Accession NM_015584) is another VGAM251 host target gene. DKFZP586F1524 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP586F1524, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586F1524 BINDING SITE, designated SEQ ID:17852, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14955] Another function of VGAM251 is therefore inhibition of DKFZP586F1524 (Accession NM_015584). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586F1524. FLJ10853 (Accession NM_018246) is another VGAM251 host target gene. FLJ10853 BINDING

SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10853, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10853 BINDING SITE, designated SEQ ID:20216, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14956] Another function of VGAM251 is therefore inhibition of FLJ10853 (Accession NM_018246). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10853. FLJ23071 (Accession NM_025192) is another VGAM251 host target gene. FLJ23071 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ23071, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23071 BINDING SITE, designated SEQ ID:24848, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14957] Another function of VGAM251 is therefore inhibition of

FLJ23071 (Accession NM_025192). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23071. KIAA0261 (Accession XM_042946) is another VGAM251 host target gene. KIAA0261 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0261, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0261 BINDING SITE, designated SEQ ID:33835, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14958] Another function of VGAM251 is therefore inhibition of KIAA0261 (Accession XM_042946). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0261. MGC2306 (Accession NM_032638) is another VGAM251 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26356, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14959] Another function of VGAM251 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. Zinc Finger Protein, Subfamily 1A, 2 (Helios) (ZNFN1A2, Accession NM_016260) is another VGAM251 host target gene. ZNFN1A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNFN1A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNFN1A2 BINDING SITE, designated SEQ ID:18389, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14960] Another function of VGAM251 is therefore inhibition of Zinc Finger Protein, Subfamily 1A, 2 (Helios) (ZNFN1A2, Accession NM_016260). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with ZNFN1A2.

LOC149603 (Accession XM_047499) is another VGAM251 host target gene. LOC149603 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149603, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149603 BINDING SITE, designated SEQ ID:34969, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14961] Another function of VGAM251 is therefore inhibition of LOC149603 (Accession XM_047499). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149603. LOC221466 (Accession XM_168087) is another VGAM251 host target gene. LOC221466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221466, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221466 BINDING SITE, designated SEQ ID:44991, to

the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14962] Another function of VGAM251 is therefore inhibition of LOC221466 (Accession XM_168087). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221466. LOC91380 (Accession XM_038134) is another VGAM251 host target gene. LOC91380 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91380, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91380 BINDING SITE, designated SEQ ID:32754, to the nucleotide sequence of VGAM251 RNA, herein designated VGAM RNA, also designated SEQ ID:2962.

[14963] Another function of VGAM251 is therefore inhibition of LOC91380 (Accession XM_038134). Accordingly, utilities of VGAM251 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91380. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 252 (VGAM252) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14964] VGAM252 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM252 was detected is described hereinabove with reference to Figs. 1–8.

[14965] VGAM252 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14966] VGAM252 gene encodes a VGAM252 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM252 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM252 precursor RNA is designated SEQ ID:238, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:238 is located at position 138077 relative to the genome of Callitrichine Herpesvirus 3.

[14967] VGAM252 precursor RNA folds onto itself, forming VGAM252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14968] An enzyme complex designated DICER COMPLEX, `dices` the VGAM252 folded precursor RNA into VGAM252 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM252 RNA is designated SEQ ID:2963, and is provided hereinbelow with reference to the sequence listing part.

[14969] VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM252 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM252 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14970] VGAM252 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM252 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM252 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14971] The complementary binding of VGAM252 RNA, herein designated VGAM RNA, to host target binding sites on VGAM252 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM252 host target RNA into VGAM252 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14972] It is appreciated that VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM252 host target genes. The mRNA of each one of this plurality of VGAM252 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM252 RNA, herein designated VGAM RNA, and which when bound by VGAM252 RNA causes inhibition of translation of respective one or more VGAM252 host target proteins.

[14973] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM252 gene, herein designated VGAM GENE, on one or more VGAM252 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14974] It is yet further appreciated that a function of VGAM252 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM252 correlate with, and may be deduced from, the identity of

the host target genes which VGAM252 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [14975] Nucleotide sequences of the VGAM252 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM252 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM252 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM252 are further described hereinbelow with reference to Table 1.
- [14976] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM252 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM252 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [14977] As mentioned hereinabove with reference to Fig. 1, a function of VGAM252 gene, herein designated VGAM is inhibition of expression of VGAM252 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM252 correlate with, and may be deduced from, the identity of the target genes which VGAM252

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[14978] Kinesin-like 1 (KNSL1, Accession NM_004523) is a VGAM252 host target gene. KNSL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KNSL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KNSL1 BINDING SITE, designated SEQ ID:10861, to the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, also designated SEQ ID:2963.

[14979] A function of VGAM252 is therefore inhibition of Kinesin-like 1 (KNSL1, Accession NM_004523), a gene which is a motor protein required for establishing a bipolar spindle. Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KNSL1. The function of KNSL1 has been established by previous studies. Kinesins are tubulin (see OMIM Ref. No. 191130) molecular motors that function to transport organelles within cells and to move chromosomes along microtubules during cell division. In sea urchin and mammalian cells, kinesins have been charac-

terized as tetrameric proteins comprising 2 heavy chains (alpha chains) of approximately 120 kD and 2 light chains (beta chains) of approximately 70 kD. The alpha chains provide the tubulin binding site and the ATPase domains, whereas the beta chains are responsible for the specific attachment of the organelle to be moved by the kinesin tetramer. Kinesins transport their bound organelle to the plus end of the microtubule. Chernajovsky et al., (1996) noted that differential splicing occurs for the kinesin beta (light) cDNA sequences at the 3-prime end of the rat kinesin mRNA, producing kinesins having different C-terminal ends that seem to confer the kinesin specificity for organelle binding. Cabeza-Arvelaiz et al. (1993) isolated and sequenced a cDNA encoding the human kinesin light chain protein (KLC). The cDNA consists of 276 nucleotides of 5-prime untranslated region, a coding sequence of 1,710 nucleotides, and 322 nucleotides of 3-prime untranslated region. It encodes a polypeptide of 569 amino acids and a deduced molecular mass of 64,789 daltons. The predicted secondary internal structure of the KLC molecule consists of about 27 contiguous repeats, each of approximately 21 amino acids, and could be divided into 3 domains. See also 601334 Chernajovsky et al.

(1996) characterized the human KNS2 gene product of a differentially spliced, T-cell-derived mRNA and cloned its promoter region. The promoter region transcribes constitutively. In permanently transfected human HeLa and NB100 neuroblastoma cells, a reporter gene containing the promoter and part of the first exon of beta kinesin was 75-fold more active than the HSV-tk promoter. The first exon contains a 5-prime untranslated sequence capable of forming a stable double-hairpin loop, which functions as a translational enhancer. Its deletion decreases the efficiency of in vitro translation of beta kinesin mRNA. Kamal et al. (2000) demonstrated that the axonal transport of APP (OMIM Ref. No. 104760) in neurons is mediated by the direct binding of APP to the kinesin light chain subunit of kinesin-I.

[14980] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[14981] Goedert, M.; Marsh, S.; Carter, N. : Localization of the human kinesin light chain gene (KNS2) to chromosome 14q32.3 by fluorescence in situ hybridization. Genomics 32: 173-175, 1996. ; and

[14982] Kamal, A.; Stokin, G. B.; Yang, Z.; Xia, C.; Goldstein, L. S. :

Axonal transport of amyloid precursor protein is mediated by direct binding to the kinesin light chain subunit of kinesin-.

[14983] Further studies establishing the function and utilities of KNSL1 are found in John Hopkins OMIM database record ID 148760, and in cited publications numbered 319 and 12000-3225 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*) (CDC14B, Accession NM_003671) is another VGAM252 host target gene. CDC14B BINDING SITE1 and CDC14B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CDC14B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDC14B BINDING SITE1 and CDC14B BINDING SITE2, designated SEQ ID:9758 and SEQ ID:27162 respectively, to the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, also designated SEQ ID:2963.

[14984] Another function of VGAM252 is therefore inhibition of CDC14 Cell Division Cycle 14 Homolog B (*S. cerevisiae*)

(CDC14B, Accession NM_003671). Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDC14B. FLJ11164 (Accession NM_018346) is another VGAM252 host target gene. FLJ11164 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ11164, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11164 BINDING SITE, designated SEQ ID:20355, to the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, also designated SEQ ID:2963.

[14985] Another function of VGAM252 is therefore inhibition of FLJ11164 (Accession NM_018346). Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11164. Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM_027679) is another VGAM252 host target gene. RHOBTB2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by RHOBTB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RHOBTB2 BINDING SITE, designated SEQ ID:30559, to the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, also designated SEQ ID:2963.

[14986] Another function of VGAM252 is therefore inhibition of Rho-related BTB Domain Containing 2 (RHOBTB2, Accession XM_027679). Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RHOBTB2. LOC150577 (Accession XM_097918) is another VGAM252 host target gene. LOC150577 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150577, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150577 BINDING SITE, designated SEQ ID:41218, to the nucleotide sequence of VGAM252 RNA, herein designated VGAM RNA, also designated SEQ ID:2963.

[14987] Another function of VGAM252 is therefore inhibition of LOC150577 (Accession XM_097918). Accordingly, utilities of VGAM252 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC150577. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 253 (VGAM253) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[14988] VGAM253 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM253 was detected is described hereinabove with reference to Figs. 1–8.

[14989] VGAM253 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[14990] VGAM253 gene encodes a VGAM253 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM253 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM253 precursor RNA is designated SEQ

ID:239, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:239 is located at position 58790 relative to the genome of Calitrichine Herpesvirus 3.

[14991] VGAM253 precursor RNA folds onto itself, forming VGAM253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[14992] An enzyme complex designated DICER COMPLEX, `dices` the VGAM253 folded precursor RNA into VGAM253 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM253 RNA is designated SEQ ID:2964, and is provided hereinbelow with reference to the sequence

listing part.

[14993] VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM253 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[14994] VGAM253 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM253 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM253 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[14995] The complementary binding of VGAM253 RNA, herein designated VGAM RNA, to host target binding sites on VGAM253 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM253 host target RNA into VGAM253 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[14996] It is appreciated that VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM253 host target genes. The mRNA of each one of this plurality of VGAM253 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM253 RNA, herein designated VGAM

RNA, and which when bound by VGAM253 RNA causes inhibition of translation of respective one or more VGAM253 host target proteins.

[14997] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM253 gene, herein designated VGAM GENE, on one or more VGAM253 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[14998] It is yet further appreciated that a function of VGAM253 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM253 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM253 correlate with, and may be deduced from, the identity of the host target genes which VGAM253 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[14999] Nucleotide sequences of the VGAM253 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM253 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM253 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM253 are further described hereinbelow with reference to Table 1.

[15000] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM253 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM253 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15001] As mentioned hereinabove with reference to Fig. 1, a function of VGAM253 gene, herein designated VGAM is

inhibition of expression of VGAM253 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM253 correlate with, and may be deduced from, the identity of the target genes which VGAM253 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15002] Calumenin (CALU, Accession NM_001219) is a VGAM253 host target gene. CALU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALU BINDING SITE, designated SEQ ID:6885, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15003] A function of VGAM253 is therefore inhibition of Calumenin (CALU, Accession NM_001219), a gene which binds 7 calcium ions with a low affinity with unidentified function. Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALU. The function of CALU has been established by previous studies. Many calcium-binding pro-

teins are reported to be localized in the endoplasmic reticulum (ER) and involved in such ER functions as protein folding and sorting. Among these are RCN1 (OMIM Ref. No. 602735), RCN2 (OMIM Ref. No. 602584), and calumenin (CALU), which form a novel family of calcium-binding proteins in the ER and Golgi apparatus. By searching sequence databases with a mouse Calu cDNA sequence (Yabe et al., 1997), Yabe et al. (1998) identified a human CALU EST, which they used to clone a full-length CALU cDNA. The cDNA encodes a deduced 315-amino acid protein containing 6 EF-hand motifs, 1 potential N-glycosylation site, and a C-terminal ER retention signal. The human and mouse CALU proteins are 98% identical. Northern blot analysis demonstrated that the 3.4-kb CALU mRNA is ubiquitously expressed in human tissues. Southern blot analysis using a human CALU cDNA probe detected bands in a variety of species. Yabe et al. (1997) mapped the mouse Calu gene to the proximal portion of chromosome 7. By fluorescence in situ hybridization, Yabe et al. (1998) localized the human CALU gene to 7q32, which was an unexpected result due to the homology of synteny between proximal mouse chromosome 7 and human 19q13.2–q13.3.

- [15004] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [15005] Yabe, D.; Nakamura, T.; Kanazawa, N.; Tashiro, K.; Honjo, T. : Calumenin, a $\text{Ca}(2+)$ -binding protein retained in the endoplasmic reticulum with a novel carboxyl-terminal sequence, HDEF. J. Biol. Chem. 272: 18232–18239, 1997. ; and
- [15006] Yabe, D.; Taniwaki, M.; Nakamura, T.; Kanazawa, N.; Tashiro, K.; Honjo, T. : Human calumenin gene (CALU): cDNA isolation and chromosomal mapping to 7q32. Genomics 49: 331–333, 1998.
- [15007] Further studies establishing the function and utilities of CALU are found in John Hopkins OMIM database record ID 603420, and in cited publications numbered 8186–8187 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Egl Nine Homolog 1 (C. elegans) (EGLN1, Accession NM_022051) is another VGAM253 host target gene. EGLN1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of EGLN1 BINDING SITE, designated SEQ ID:22585, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15008] Another function of VGAM253 is therefore inhibition of Egl Nine Homolog 1 (*C. elegans*) (EGLN1, Accession NM_022051), a gene which is expressed in the cytoplasm of arterial smooth muscle cells. Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGLN1. The function of EGLN1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM216.FLJ11155 (Accession NM_018342) is another VGAM253 host target gene. FLJ11155 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11155, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11155 BINDING SITE, designated SEQ ID:20348, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15009] Another function of VGAM253 is therefore inhibition of FLJ11155 (Accession NM_018342). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11155. FLJ12697 (Accession XM_166526) is another VGAM253 host target gene. FLJ12697 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12697 BINDING SITE, designated SEQ ID:44473, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15010] Another function of VGAM253 is therefore inhibition of FLJ12697 (Accession XM_166526). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12697. KIAA1023 (Accession NM_017604) is another VGAM253 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19091, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15011] Another function of VGAM253 is therefore inhibition of KIAA1023 (Accession NM_017604). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. KIAA1941 (Accession XM_059318) is another VGAM253 host target gene. KIAA1941 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1941, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1941 BINDING SITE, designated SEQ ID:36952, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15012] Another function of VGAM253 is therefore inhibition of KIAA1941 (Accession XM_059318). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1941. LOC149912 (Accession XM_097743) is another VGAM253 host target gene. LOC149912 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC149912, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149912 BINDING SITE, designated SEQ ID:41087, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15013] Another function of VGAM253 is therefore inhibition of LOC149912 (Accession XM_097743). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149912. LOC155179 (Accession XM_088169) is another VGAM253 host target gene. LOC155179 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155179, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155179 BINDING SITE, designated SEQ ID:39558, to the nucleotide sequence of VGAM253 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2964.

[15014] Another function of VGAM253 is therefore inhibition of LOC155179 (Accession XM_088169). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155179. LOC199958 (Accession XM_117163) is another VGAM253 host target gene. LOC199958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199958 BINDING SITE, designated SEQ ID:43266, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15015] Another function of VGAM253 is therefore inhibition of LOC199958 (Accession XM_117163). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199958. LOC219731 (Accession XM_167596) is another VGAM253 host target gene. LOC219731 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219731, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219731 BINDING SITE, designated SEQ ID:44718, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15016] Another function of VGAM253 is therefore inhibition of LOC219731 (Accession XM_167596). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219731. LOC254735 (Accession XM_171051) is another VGAM253 host target gene. LOC254735 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254735, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254735 BINDING SITE, designated SEQ ID:45838, to the nucleotide sequence of VGAM253 RNA, herein designated VGAM RNA, also designated SEQ ID:2964.

[15017] Another function of VGAM253 is therefore inhibition of LOC254735 (Accession XM_171051). Accordingly, utilities of VGAM253 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC254735. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 254 (VGAM254) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15018] VGAM254 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM254 was detected is described hereinabove with reference to Figs. 1–8.

[15019] VGAM254 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15020] VGAM254 gene encodes a VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM254 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM254 precursor RNA is designated SEQ

ID:240, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:240 is located at position 17777 relative to the genome of Calitrichine Herpesvirus 3.

[15021] VGAM254 precursor RNA folds onto itself, forming VGAM254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15022] An enzyme complex designated DICER COMPLEX, `dices` the VGAM254 folded precursor RNA into VGAM254 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 83%) nucleotide sequence of VGAM254 RNA is designated SEQ ID:2965, and is provided hereinbelow with reference to the sequence

listing part.

[15023] VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM254 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15024] VGAM254 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM254 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM254 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15025] The complementary binding of VGAM254 RNA, herein designated VGAM RNA, to host target binding sites on VGAM254 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM254 host target RNA into VGAM254 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15026] It is appreciated that VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM254 host target genes. The mRNA of each one of this plurality of VGAM254 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM254 RNA, herein designated VGAM

RNA, and which when bound by VGAM254 RNA causes inhibition of translation of respective one or more VGAM254 host target proteins.

[15027] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM254 gene, herein designated VGAM GENE, on one or more VGAM254 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15028] It is yet further appreciated that a function of VGAM254 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM254 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM254 correlate with, and may be deduced from, the identity of the host target genes which VGAM254 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15029] Nucleotide sequences of the VGAM254 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM254 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM254 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM254 are further described hereinbelow with reference to Table 1.

[15030] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM254 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM254 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15031] As mentioned hereinabove with reference to Fig. 1, a function of VGAM254 gene, herein designated VGAM is

inhibition of expression of VGAM254 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM254 correlate with, and may be deduced from, the identity of the target genes which VGAM254 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15032] Fibrillin 2 (congenital contractural arachnodactyly) (FBN2, Accession NM_001999) is a VGAM254 host target gene. FBN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBN2 BINDING SITE, designated SEQ ID:7725, to the nucleotide sequence of VGAM254 RNA, herein designated VGAM RNA, also designated SEQ ID:2965.

[15033] A function of VGAM254 is therefore inhibition of Fibrillin 2 (congenital contractural arachnodactyly) (FBN2, Accession NM_001999), a gene which structural component of connective tissue microfibrils that binds calcium. fibrillin-2-containing microfibrils regulate the early process of elastic fiber assembly. Accordingly, utilities of VGAM254 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with FBN2. The function of FBN2 has been established by previous studies. Beals and Hecht (1971) described father and 2 sons affected in 1 kindred and father, daughter and son (by different mothers) affected in a second kindred. They proposed that the disorder be called 'contractural arachnodactyly' and further suggested that the patient reported by Marfan (1896) had this disorder rather than the Marfan syndrome (OMIM Ref. No. 154700) as presently delineated (Hecht and Beals, 1972). They found several other reports, apparently of the same disorder. Beyer et al. (1965) probably described the same condition in a mother and 4 children and some of the reports of combined Marfan syndrome and arthrogryposis multiplex congenita may be further examples (e.g., Reeve et al., 1960; Kingsley-Pillers, 1946). Epstein et al. (1968) described father and son with a connective tissue disorder with some features suggesting the Marfan syndrome and some suggesting osteogenesis imperfecta. Severe kyphoscoliosis, generalized osteopenia, flexion contractures of the fingers and abnormally shaped ears were among the characteristics. Abnormally shaped ('crumpled') ears have been emphasized by other students of CCA. According to Mirise and Shear (1979), the ocular

and cardiovascular complications of the Marfan syndrome do not occur in contractural arachnodactyly (Mirise and Shear, 1979). Hence, the correct diagnosis has prognostic significance. Park et al. (1998) identified FBN2 mutations in 6 of 12 unrelated CCA patient cell strains. All of the identified mutations were clustered in a limited region of the gene, a region corresponding to that in FBN1 where mutations produce the severe, congenital form of Marfan syndrome, so-called neonatal Marfan syndrome. Furthermore, 3 of the identified mutations occurred in the FBN2 locations exactly corresponding to FBN1 mutations that had been reported in cases of neonatal Marfan syndrome. These mutations indicate that this central region of both fibrillins plays a critical role in human embryogenesis. The limited region of FBN2 that can be mutated to cause CCA may also help explain the rarity of CCA compared to Marfan syndrome. Belleh et al. (2000) reported 2 additional FBN2 mutations in CCA: C1141F in exon 26 (121050.0008) and C1252W in exon 29 (121050.0009). As in previous cases, mutations clustered in the region of fibrillin-2 homologous to the so-called neonatal Marfan syndrome region of fibrillin-1 (FBN1; 134797) (Kainulainen et al., 1994). Gupta et al. (2002) noted that

all of the identified CCA mutations in FBN2 cluster in a limited region similar to that where severe Marfan syndrome mutations cluster in FBN1, specifically between exons 23 and 34. Gupta et al. (2002) screened exons 22 through 36 of FBN2 for mutations in 13 patients with classic CCA by single-stranded conformation polymorphism analysis followed by direct sequencing. They successfully identified 10 novel mutations in this critical region of FBN2 in these patients, indicating a mutation detection rate of 75% in this region. None of these identified FBN2 mutations alter amino acids in the calcium-binding consensus sequence in the EGF-like domains, whereas many of the FBN1 mutations alter the consensus sequence. Gupta et al. (2002) reviewed the 21 known CAA mutations in the FBN2 gene, along with available clinical information on the probands. They found that 3 of the 21 patients had dilatation of the aortic root. All 3 were young, and the degree of dilatation appeared to have been borderline in all. However, because of the lack of knowledge of the natural history of aortic involvement in CCA, Gupta et al. (2002) recommended that all CCA patients have an echocardiogram. They cited Su et al. (2000) as indicating that approximately 15% of CCA patients have

congenital heart defects. Their review did not support this conclusion, instead suggesting that congenital heart defects are only an occasional finding in these patients. Animal model experiments lend further support to the function of FBN2. Chaudhry et al. (2001) analyzed the classic mouse mutant 'Shaker-with-syndactylism' (sy) using a positional candidate approach. The authors demonstrated that several loss-of-function mutations, each located outside the 'neonatal region' of Fbn2, caused syndactyly in mice, rather than CCA as in man. The deafness in these animals is caused by mutations in the contiguous Na-K-2Cl cotransporter gene Slc12a2 (OMIM Ref. No. 600840) (Dixon et al., 1999).

[15034] It is appreciated that the abovementioned animal model for FBN2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15035] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15036] Gupta, P. A.; Putnam, E. A.; Carmical, S. G.; Kaitila, I.; Steinmann, B.; Child, A.; Danesino, C.; Metcalfe, K.; Berry, S. A.; Chen, E.; Delorme, C. V.; Thong, M.-K.; Ades, L. C.;

Milewicz, D. M. : Ten novel FBN2 mutations in congenital contractural arachnodactyly: delineation of the molecular pathogenesis and clinical phenotype. Hum. Mutat. 19: 39–48, 2002. ; and

[15037] Su, P.–H.; Hou, J.–W.; Hwu, W.–L.; Wu, M.–H.; Wang, J.–K.; Wang, T.–R. : Congenital contractural arachnodactyly (Beals syndrome). Acta Paediat. 41: 59–62, 2000.

[15038] Further studies establishing the function and utilities of FBN2 are found in John Hopkins OMIM database record ID 121050, and in cited publications numbered 148–149, 298–309, 313, 314–312, 315–330, 38 and 4654–4661 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Juncctophilin 3 (JPH3, Accession NM_020655) is another VGAM254 host target gene. JPH3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by JPH3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JPH3 BINDING SITE, designated SEQ ID:21827, to the nucleotide sequence of VGAM254 RNA, herein designated VGAM RNA, also designated SEQ ID:2965.

[15039] Another function of VGAM254 is therefore inhibition of Junctophilin 3 (JPH3, Accession NM_020655), a gene which is involved in cytoskeletal organization and cellular growth. Accordingly, utilities of VGAM254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JPH3. The function of JPH3 has been established by previous studies. Junctional complexes between the plasma membrane (PM) and endoplasmic/sarcoplasmic reticulum (ER/SR) are a common feature of all excitable cell types and mediate cross talk between cell surface and intracellular ion channels. Takeshima et al. (2000) identified the junctophilins (JPs), a conserved family of proteins that are components of the junctional complexes. JPs are composed of a C-terminal hydrophobic segment spanning the ER/SR membrane and a remaining cytoplasmic domain that shows specific affinity for the PM. In mouse, there are at least 3 JP subtypes: Jp1, Jp2, and Jp3 Margolis et al. (2001) described a disorder termed Huntington disease-like 2 (HDL2; 606438) segregating in an autosomal dominant pattern in a large pedigree with an unidentified CAG/CTG expansion. Holmes et al. (2001) reported the cloning of this expansion and its localization to a variably spliced exon of JPH3, a gene involved in the

formation of junctional membrane structures. They stated the location of the gene as 16q24.3. All 10 affected individuals tested had a repeat expansion, ranging in size from 51 to 57 triplets, whereas 3 unaffected individuals had 2 unexpanded alleles. The variability of the length of the expanded repeat among sibs from 3 different sibships indicated that the expanded allele is unstable in vertical transmission. There was no apparent correlation between repeat size and age of onset, but the range of repeat length among family members was narrow. The index family was African-American; Holmes et al. (2001) detected HDL2-related repeat expansions in 4 African-American individuals from the southeastern United States, each of whom had a familial Huntington disease-like disorder and had tested negative for the Huntington disease mutation. They demonstrated that the CTG repeat is localized 760 nucleotides 3-prime to the end of exon 1. At least 4 lines of evidence suggested that the CTG repeat is contained within an alternatively spliced exon (termed 2A) of the JPH3 gene that has multiple splice acceptor sites.

[15040] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [15041] Holmes, S. E.; O'Hearn, E.; Rosenblatt, A.; Callahan, C.; Hwang, H. S.; Ingersoll-Ashworth, R. G.; Fleisher, A.; Stevanin, G.; Brice, A.; Potter, N. T.; Ross, C. A.; Margolis, R. L. : A repeat expansion in the gene encoding junctophilin-3 is associated with Huntington disease-like 2. *Nature Genet.* 29: 377-378, 2001. Note: Erratum: *Nature Genet.* 30: 123 only, 2002. ; and
- [15042] Margolis, R. L.; O'Hearn, E.; Rosenblatt, A.; Willour, V.; Holmes, S. E.; Franz, M. L.; Callahan, C.; Hwang, H. S.; Troncoso, J. C.; Ross, C. A. : A disorder similar to Huntington's dis.
- [15043] Further studies establishing the function and utilities of JPH3 are found in John Hopkins OMIM database record ID 605268, and in cited publications numbered 503 and 5036-5037 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LOC145371 (Accession XM_085123) is another VGAM254 host target gene. LOC145371 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC145371 BINDING SITE, designated SEQ ID:37843, to the nucleotide sequence of VGAM254 RNA, herein designated VGAM RNA, also designated SEQ ID:2965.

[15044] Another function of VGAM254 is therefore inhibition of LOC145371 (Accession XM_085123). Accordingly, utilities of VGAM254 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145371. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 255 (VGAM255) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15045] VGAM255 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM255 was detected is described hereinabove with reference to Figs. 1–8.

[15046] VGAM255 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15047] VGAM255 gene encodes a VGAM255 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM255 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM255 precursor RNA is designated SEQ ID:241, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:241 is located at position 113673 relative to the genome of Calitrichine Herpesvirus 3.

[15048] VGAM255 precursor RNA folds onto itself, forming VGAM255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15049] An enzyme complex designated DICER COMPLEX, `dices` the VGAM255 folded precursor RNA into VGAM255 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM255 RNA is designated SEQ ID:2966, and is provided hereinbelow with reference to the sequence listing part.

[15050] VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM255 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15051] VGAM255 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM255 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM255 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15052] The complementary binding of VGAM255 RNA, herein designated VGAM RNA, to host target binding sites on VGAM255 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM255 host target RNA into VGAM255 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15053] It is appreciated that VGAM255 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM255 host target genes. The mRNA of each one of this plurality of VGAM255 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM255 RNA, herein designated VGAM RNA, and which when bound by VGAM255 RNA causes inhibition of translation of respective one or more VGAM255 host target proteins.

[15054] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM255 gene, herein designated VGAM GENE, on one or more VGAM255 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[15055] It is yet further appreciated that a function of VGAM255 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM255 correlate with, and may be deduced from, the identity of the host target genes which VGAM255 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15056] Nucleotide sequences of the VGAM255 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM255 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM255 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM255 are further described hereinbelow with reference to Table 1.

[15057] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM255 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM255 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15058] As mentioned hereinabove with reference to Fig. 1, a function of VGAM255 gene, herein designated VGAM is inhibition of expression of VGAM255 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM255 correlate with, and may be deduced from, the identity of the target genes which VGAM255 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15059] UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 6 (B4GALT6, Accession XM_008799) is a VGAM255 host target gene. B4GALT6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by B4GALT6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of B4GALT6 BINDING SITE, designated SEQ ID:30095, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15060] A function of VGAM255 is therefore inhibition of UDP-Gal:betaGlcNAc Beta 1,4- Galactosyltransferase, Polypeptide 6 (B4GALT6, Accession XM_008799). Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with B4GALT6. Chemokine (C-C motif) Receptor 2 (CCR2, Accession NM_000648) is another VGAM255 host target gene. CCR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCR2 BINDING SITE, designated SEQ ID:6312, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15061] Another function of VGAM255 is therefore inhibition of Chemokine (C-C motif) Receptor 2 (CCR2, Accession NM_000648), a gene which binds chemokines and transduces a signal by increasing the intracellular calcium ions level. Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCR2. The function of CCR2 and its association with various diseases and clinical conditions,

has been established by previous studies, as described hereinabove with reference to VGAM206. Kruppel-like Factor 5 (intestinal) (KLF5, Accession NM_001730) is another VGAM255 host target gene. KLF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLF5 BINDING SITE, designated SEQ ID:7463, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15062] Another function of VGAM255 is therefore inhibition of Kruppel-like Factor 5 (intestinal) (KLF5, Accession NM_001730). Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLF5. N-acetylated Alpha-linked Acidic Dipeptidase 2 (NAALAD2, Accession NM_005467) is another VGAM255 host target gene. NAALAD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAALAD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of NAALAD2 BINDING SITE, designated SEQ ID:11963, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15063] Another function of VGAM255 is therefore inhibition of N-acetylated Alpha-linked Acidic Dipeptidase 2 (NAALAD2, Accession NM_005467). Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAALAD2. Progesterone Receptor Membrane Component 2 (PGRMC2, Accession NM_006320) is another VGAM255 host target gene. PGRMC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PGRMC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PGRMC2 BINDING SITE, designated SEQ ID:13012, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15064] Another function of VGAM255 is therefore inhibition of Progesterone Receptor Membrane Component 2 (PGRMC2,

Accession NM_006320). Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PGRMC2.

LOC92270 (Accession XM_043989) is another VGAM255 host target gene. LOC92270 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92270, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92270 BINDING SITE, designated SEQ ID:34061, to the nucleotide sequence of VGAM255 RNA, herein designated VGAM RNA, also designated SEQ ID:2966.

[15065] Another function of VGAM255 is therefore inhibition of LOC92270 (Accession XM_043989). Accordingly, utilities of VGAM255 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92270. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 256 (VGAM256) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[15066] VGAM256 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM256 was detected is described hereinabove with reference to Figs. 1–8.

[15067] VGAM256 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15068] VGAM256 gene encodes a VGAM256 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM256 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM256 precursor RNA is designated SEQ ID:242, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:242 is located at position 43629 relative to the genome of Callitrichine Herpesvirus 3.

[15069] VGAM256 precursor RNA folds onto itself, forming VGAM256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[15070] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM256 folded precursor RNA into VGAM256 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 70%) nucleotide se-
quence of VGAM256 RNA is designated SEQ ID:2967, and
is provided hereinbelow with reference to the sequence
listing part.

[15071] VGAM256 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM256 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM256 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15072] VGAM256 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM256 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM256 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[15073] The complementary binding of VGAM256 RNA, herein designated VGAM RNA, to host target binding sites on VGAM256 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM256 host target RNA into VGAM256 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15074] It is appreciated that VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM256 host target genes. The mRNA of each one of this plurality of VGAM256 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM256 RNA, herein designated VGAM RNA, and which when bound by VGAM256 RNA causes inhibition of translation of respective one or more VGAM256 host target proteins.

[15075] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM256 gene, herein designated VGAM GENE, on one or

more VGAM256 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15076] It is yet further appreciated that a function of VGAM256 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM256 correlate with, and may be deduced from, the identity of the host target genes which VGAM256 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [15077] Nucleotide sequences of the VGAM256 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM256 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM256 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM256 are further described hereinbelow with reference to Table 1.
- [15078] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM256 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM256 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [15079] As mentioned hereinabove with reference to Fig. 1, a function of VGAM256 gene, herein designated VGAM is inhibition of expression of VGAM256 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM256 correlate with, and may be deduced from, the identity of the target genes which VGAM256 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [15080] Carnitine O-octanoyltransferase (CROT, Accession

NM_021151) is a VGAM256 host target gene. CROT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CROT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CROT BINDING SITE, designated SEQ ID:22125, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15081] A function of VGAM256 is therefore inhibition of Carnitine O-octanoyltransferase (CROT, Accession NM_021151), a gene which CROT plays a crucial role in the beta-oxidation of branched-chain fatty acids including pristanic acid. Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CROT. The function of CROT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM70.D10S170 (Accession NM_005436) is another VGAM256 host target gene. D10S170 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by D10S170, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D10S170 BINDING SITE, designated SEQ ID:11920, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15082] Another function of VGAM256 is therefore inhibition of D10S170 (Accession NM_005436), a gene which may provide a structural basis for generation of RET/PTC1 rearrangement . Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D10S170. The function of D10S170 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM142.MHC Class II Transactivator (MHC2TA, Accession NM_000246) is another VGAM256 host target gene. MHC2TA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MHC2TA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MHC2TA BINDING SITE, designated SEQ

ID:5776, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15083] Another function of VGAM256 is therefore inhibition of MHC Class II Transactivator (MHC2TA, Accession NM_000246). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MHC2TA. Neuroligin 2 (NLGN2, Accession XM_113932) is another VGAM256 host target gene. NLGN2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NLGN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NLGN2 BINDING SITE, designated SEQ ID:42551, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15084] Another function of VGAM256 is therefore inhibition of Neuroligin 2 (NLGN2, Accession XM_113932), a gene which rapidly hydrolyzes choline released into the synapse. Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical

conditions associated with NLGN2. The function of NLGN2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Src Family Associated Phosphoprotein 2 (SCAP2, Accession NM_003930) is another VGAM256 host target gene. SCAP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCAP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCAP2 BINDING SITE, designated SEQ ID:10030, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15085] Another function of VGAM256 is therefore inhibition of Src Family Associated Phosphoprotein 2 (SCAP2, Accession NM_003930), a gene which interacts with Src family protein tyrosine kinases and SLAP/FYB (SLA). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCAP2. The function of SCAP2 and its association with various diseases and clinical conditions, has been es-

established by previous studies, as described hereinabove with reference to VGAM134.DKFZP566M114 (Accession NM_032128) is another VGAM256 host target gene. DKFZP566M114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP566M114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP566M114 BINDING SITE, designated SEQ ID:25814, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15086] Another function of VGAM256 is therefore inhibition of DKFZP566M114 (Accession NM_032128). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP566M114. FLJ22833 (Accession NM_022837) is another VGAM256 host target gene. FLJ22833 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22833, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ22833 BINDING SITE, designated SEQ ID:23123, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15087] Another function of VGAM256 is therefore inhibition of FLJ22833 (Accession NM_022837). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22833. LHX6 (Accession NM_014368) is another VGAM256 host target gene. LHX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LHX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHX6 BINDING SITE, designated SEQ ID:15698, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15088] Another function of VGAM256 is therefore inhibition of LHX6 (Accession NM_014368). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHX6. Protein Serine Kinase H1 (PSKH1, Accession XM_043047) is another VGAM256 host target gene. PSKH1 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PSKH1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSKH1 BINDING SITE, designated SEQ ID:33869, to the nucleotide sequence of VGAM256 RNA, herein designated VGAM RNA, also designated SEQ ID:2967.

[15089] Another function of VGAM256 is therefore inhibition of Protein Serine Kinase H1 (PSKH1, Accession XM_043047). Accordingly, utilities of VGAM256 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PSKH1. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 257 (VGAM257) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15090] VGAM257 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM257 was detected is described hereinabove with reference to Figs. 1-8.

[15091] VGAM257 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15092] VGAM257 gene encodes a VGAM257 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM257 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM257 precursor RNA is designated SEQ ID:243, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:243 is located at position 100658 relative to the genome of Callitrichine Herpesvirus 3.

[15093] VGAM257 precursor RNA folds onto itself, forming VGAM257 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[15094] An enzyme complex designated DICER COMPLEX, `dices` the VGAM257 folded precursor RNA into VGAM257 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM257 RNA is designated SEQ ID:2968, and is provided hereinbelow with reference to the sequence listing part.

[15095] VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM257 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15096] VGAM257 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM257 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM257 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM257 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15097] The complementary binding of VGAM257 RNA, herein designated VGAM RNA, to host target binding sites on VGAM257 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM257 host target RNA into VGAM257 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15098] It is appreciated that VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM257 host target genes. The mRNA of each one of this plurality of VGAM257 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM257 RNA, herein designated VGAM RNA, and which when bound by VGAM257 RNA causes inhibition of translation of respective one or more VGAM257 host target proteins.

[15099] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM257 gene, herein designated VGAM GENE, on one or more VGAM257 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15100] It is yet further appreciated that a function of VGAM257 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM257 correlate with, and may be deduced from, the identity of the host target genes which VGAM257 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15101] Nucleotide sequences of the VGAM257 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM257 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM257 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM257 are further described hereinbelow with reference to Table 1.

[15102] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM257 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM257 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15103] As mentioned hereinabove with reference to Fig. 1, a function of VGAM257 gene, herein designated VGAM is inhibition of expression of VGAM257 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM257 correlate with, and may be deduced from, the identity of the target genes which VGAM257 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15104] Caspase 4, Apoptosis-related Cysteine Protease (CASP4, Accession NM_033307) is a VGAM257 host target gene. CASP4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CASP4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of CASP4 BINDING SITE, designated SEQ ID:27142, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15105] A function of VGAM257 is therefore inhibition of Caspase 4, Apoptosis-related Cysteine Protease (CASP4, Accession NM_033307), a gene which is an apoptosis-related caspase and involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP4. The function of CASP4 has been established by previous studies. Cysteine proteases related to mammalian interleukin-1-beta converting enzyme (ICE; 147678) and nematode CED3 have been implicated in apoptotic cell death. By screening a human thymus cDNA library with the human ICE coding sequence, Kamens et al. (1995) isolated cDNAs encoding CASP4, named ICH2 (ICE and CED3 homolog-2) by them. The 377-amino acid ICH2 protein has 53% amino acid identity with ICE and contains the residues conserved in all ICE family members. ICH2 and ICE share catalytic properties but may differ in substrate

specificities, suggesting that the 2 enzymes have different functions in vivo. Overexpression of ICH2 in insect cells induced apoptosis. By Northern blot analysis, ICH2 was expressed as an approximately 1.7-kb transcript in all tissues examined, with the exception of brain. The ICH2 coding sequence is contained within 8 exons. The authors mapped the ICH2 gene to a P1 clone containing the ICE gene, which is located at 11q22.2–q22.3. Animal model experiments lend further support to the function of CASP4. Wang et al. (1998) reported the inactivation of mouse casp11, which is most homologous to human CASP4, by gene targeting. Like Ice-deficient mice, casp11 mutant mice are resistant to endotoxic shock induced by lipopolysaccharide. Production of both IL1- α and IL1- β after lipopolysaccharide stimulation, a crucial event during septic shock and an indication of ICE activation, is blocked in casp11 mutant mice. Casp11 mutant embryonic fibroblast cells are resistant to apoptosis induced by overexpression of ICE. Furthermore, Wang et al. (1998) found that pro-caspase-11 physically interacts with pro-ICE in cells and that the expression of casp11 is essential for activation of ICE. The authors suggested that caspase-11 is a component of the ICE complex and is re-

quired for the activation of ICE.

[15106] It is appreciated that the abovementioned animal model for CASP4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15107] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15108] Wang, S.; Miura, M.; Jung, Y.; Zhu, H.; Li, E.; Yuan, J. : Murine caspase-11, an ICE-interacting protease, is essential for the activation of ICE. Cell 92: 501-509, 1998. ; and

[15109] Kamens, J.; Paskind, M.; Hugunin, M.; Talanian, R. V.; Allen, H.; Banach, D.; Bump, N.; Hackett, M.; Johnston, C. G.; Li, P.; Mankovich, J. A.; Terranova, M.; Ghayur, T. : Identification.

[15110] Further studies establishing the function and utilities of CASP4 are found in John Hopkins OMIM database record ID 602664, and in cited publications numbered 5915-591 and 5913-5914 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Major Histocompatibility Complex, Class II, DQ Alpha 1 (HLA-DQA1, Accession XM_175260) is another VGAM257 host target gene. HLA-DQA1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HLA-DQA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HLA-DQA1 BINDING SITE, designated SEQ ID:46727, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15111] Another function of VGAM257 is therefore inhibition of Major Histocompatibility Complex, Class II, DQ Alpha 1 (HLA-DQA1, Accession XM_175260), a gene which is alpha 1 chain of HLA-DQ1 class II molecule (Ia antigen) which binds peptides and presents them to CD4+ T lymphocytes. Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HLA-DQA1. The function of HLA-DQA1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM132.FLJ11210 (Accession XM_005298) is another VGAM257 host target gene. FLJ11210 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11210, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11210 BINDING SITE, designated SEQ ID:29972, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15112] Another function of VGAM257 is therefore inhibition of FLJ11210 (Accession XM_005298). Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11210. FLJ14564 (Accession XM_084459) is another VGAM257 host target gene. FLJ14564 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14564, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14564 BINDING SITE, designated SEQ ID:37599, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15113] Another function of VGAM257 is therefore inhibition of FLJ14564 (Accession XM_084459). Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with FLJ14564. KIAA1854 (Accession XM_049884) is another VGAM257 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35527, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15114] Another function of VGAM257 is therefore inhibition of KIAA1854 (Accession XM_049884). Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. PIP3-E (Accession XM_039749) is another VGAM257 host target gene. PIP3-E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP3-E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP3-E BINDING SITE, designated SEQ ID:33178, to the nucleotide sequence of

VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15115] Another function of VGAM257 is therefore inhibition of PIP3-E (Accession XM_039749). Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP3-E. LOC135932 (Accession XM_072433) is another VGAM257 host target gene. LOC135932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135932 BINDING SITE, designated SEQ ID:37499, to the nucleotide sequence of VGAM257 RNA, herein designated VGAM RNA, also designated SEQ ID:2968.

[15116] Another function of VGAM257 is therefore inhibition of LOC135932 (Accession XM_072433). Accordingly, utilities of VGAM257 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135932. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 258 (VGAM258) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15117] VGAM258 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM258 was detected is described hereinabove with reference to Figs. 1–8.

[15118] VGAM258 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15119] VGAM258 gene encodes a VGAM258 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM258 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM258 precursor RNA is designated SEQ ID:244, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:244 is located at position 29168 relative to the genome of Callitrichine Herpesvirus 3.

[15120] VGAM258 precursor RNA folds onto itself, forming VGAM258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15121] An enzyme complex designated DICER COMPLEX, `dices` the VGAM258 folded precursor RNA into VGAM258 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM258 RNA is designated SEQ ID:2969, and is provided hereinbelow with reference to the sequence listing part.

[15122] VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM258 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM258 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15123] VGAM258 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM258 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM258 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15124] The complementary binding of VGAM258 RNA, herein designated VGAM RNA, to host target binding sites on VGAM258 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM258 host target RNA into VGAM258 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15125] It is appreciated that VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM258 host target genes. The mRNA of each one of this plurality of VGAM258 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM258 RNA, herein designated VGAM RNA, and which when bound by VGAM258 RNA causes inhibition of translation of respective one or more VGAM258 host target proteins.

[15126] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM258 gene, herein designated VGAM GENE, on one or more VGAM258 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15127] It is yet further appreciated that a function of VGAM258 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM258 correlate with, and may be deduced from, the identity of

the host target genes which VGAM258 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [15128] Nucleotide sequences of the VGAM258 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM258 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM258 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM258 are further described hereinbelow with reference to Table 1.
- [15129] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM258 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM258 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [15130] As mentioned hereinabove with reference to Fig. 1, a function of VGAM258 gene, herein designated VGAM is inhibition of expression of VGAM258 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM258 correlate with, and may be deduced from, the identity of the target genes which VGAM258

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15131] Heat Shock 70kDa Protein 8 (HSPA8, Accession NM_006597) is a VGAM258 host target gene. HSPA8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HSPA8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPA8 BINDING SITE, designated SEQ ID:13369, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15132] A function of VGAM258 is therefore inhibition of Heat Shock 70kDa Protein 8 (HSPA8, Accession NM_006597), a gene which acts as a chaperone. plays an important role in cells by transiently associating with nascent polypeptides to facilitate correct folding. Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPA8. The function of HSPA8 has been established by previous studies. Cytokine and protooncogene mRNAs are rapidly degraded through AU-rich elements in the 3-prime untranslated region. Rapid decay involves AU-rich binding

protein AUF1, which complexes with heat-shock proteins HSC70 and HSP70, translation initiation factor EIF4G (OMIM Ref. No. 600495), and poly(A)-binding protein (OMIM Ref. No. 604679). AU-rich mRNA decay is associated with displacement of EIF4G from AUF1, ubiquitination of AUF1, and degradation of AUF1 by proteasomes. Induction of HSP70 by heat shock, downregulation of the ubiquitin-proteasome network, or inactivation of ubiquitinating enzyme E1 (OMIM Ref. No. 314370), all result in HSP70 sequestration of AUF1 in the perinucleus-nucleus, and all 3 processes block decay of AU-rich mRNAs and AUF1 protein. These results link the rapid degradation of cytokine mRNAs to the ubiquitin-proteasome pathway (Larola et al., 1999). CD14 (OMIM Ref. No. 158120) and lipopolysaccharide (LPS)-binding protein (LBP; 151990) are major receptors for LPS; however, binding analyses and TNF production assays have suggested the presence of additional cell surface receptors, designated LPS-associated proteins (LAPs), that are distinct from CD14, LBP, and the Toll-like receptors (see OMIM Ref. No. TLR4; 603030). Using affinity chromatography, peptide mass fingerprinting, and fluorescence resonance energy transfer, Triantafilou et al. (2001) identified 4 diverse proteins,

heat shock cognate protein (HSPA8), HSP90A, chemokine receptor CXCR4 (OMIM Ref. No. 162643), and growth differentiation factor-5 (GDF5; 601146), on monocytes that form an activation cluster after LPS ligation and are involved in LPS signal transduction. Antibody inhibition analysis suggested that disruption of cluster formation abrogates TNF release. Triantafilou et al. (2001) proposed that heat shock proteins, which are highly conserved from bacteria to eukaryotic cells, are remnants of an ancient system of antigen presentation and defense against microbial pathogens.

- [15133] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [15134] Larola, G.; Cuesta, R.; Brewer, G.; Schneider, R. J. : Control of mRNA decay by heat shock-ubiquitin-proteasome pathway. *Science* 284: 499-502, 1999. ; and
- [15135] Triantafilou, K.; Triantafilou, M.; Dedrick, R. L. : A CD14-independent LPS receptor cluster. *Nature Immun.* 2: 338-345, 2001.
- [15136] Further studies establishing the function and utilities of HSPA8 are found in John Hopkins OMIM database record ID 600816, and in cited publications numbered

7522–7523, 821 and 12001 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 24 (IL24, Accession NM_006850) is another VGAM258 host target gene. IL24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL24 BINDING SITE, designated SEQ ID:13719, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15137] Another function of VGAM258 is therefore inhibition of Interleukin 24 (IL24, Accession NM_006850), a gene which may contribute to terminal cell differentiation. Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL24. The function of IL24 has been established by previous studies. Jiang et al. (1995) used a differentiation induction subtraction hybridization strategy to identify and clone genes involved in growth control and terminal differentiation in human cancer cells. By this approach they identified melanoma differentiation-associated gene–

7 (MDA7), whose expression is upregulated as a consequence of terminal differentiation in human melanoma cells. Forced expression of MDA7 was found to be growth inhibitory toward diverse human tumor cells (Jiang et al., 1996). Huang et al. (2001) determined that the human MDA7 gene encodes a protein with a predicted size of 23.8 kD, consisting of 206 amino acids. They concluded that MDA7 represents a differentiation-, growth-, and apoptosis-associated gene with potential utility for the gene-based therapy of diverse human cancers. Animal model experiments lend further support to the function of IL24. IL24 selectively suppresses the growth of human breast cancer cells and the consequence of ectopic expression of MDA7 on human breast tumor formation in vivo in nude mice.

[15138] It is appreciated that the abovementioned animal model for IL24 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15139] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15140] Huang, E. Y.; Madireddi, M. T.; Gopalkrishnan, R. V.;

Leszczyniecka, M.; Su, Z.; Lebedeva, I. V.; Kang, D.; Jiang, H.; Lin, J. J.; Alexandre, D.; Chen, Y.; Vozhilla, N. : {and 9 others}: Genomic structure, chromosomal localization and expression profile of a novel melanoma differentiation associated (mda-7) gene with cancer specific growth suppressing and apoptosis inducing properties. *Oncogene* 20: 7051-7063, 2001. ; and

[15141] Jiang, H.; Lin, J. J.; Su, Z.-Z.; Goldstein, N. I.; Fisher, P. B. : Subtraction hybridization identifies a novel melanoma differentiation associated gene, mda-7, modulated during human.

[15142] Further studies establishing the function and utilities of IL24 are found in John Hopkins OMIM database record ID 604136, and in cited publications numbered 4438-4442 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ligase IV, DNA, ATP-dependent (LIG4, Accession NM_002312) is another VGAM258 host target gene. LIG4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LIG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIG4 BINDING SITE, desig-

nated SEQ ID:8108, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15143] Another function of VGAM258 is therefore inhibition of Ligase IV, DNA, ATP-dependent (LIG4, Accession NM_002312), a gene which functions in DNA nonhomologous end-joining and V(D)J recombination. Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIG4. The function of LIG4 has been established by previous studies. Grawunder et al. (1998) showed that targeted disruption of both DNA ligase IV alleles in a human pre-B cell line rendered the cells sensitive to ionizing radiation and ablated V(D)J recombination. This phenotype could only be reversed by complementation with DNA ligase IV but not by expression of either of the remaining 2 ligases, DNA ligase I or III. Hence, DNA ligase IV is the activity responsible for the ligation step in nonhomologous DNA end joining and in V(D)J recombination. Animal model experiments lend further support to the function of LIG4. In mice, Lig4 deficiency causes embryonic lethality, massive neuronal apoptosis, arrested lymphogenesis, and various cellular defects (Frank et al., 1998). Frank et al.

(2000) assessed potential roles in this phenotype for INK4a/ARF (CDKN2A; 600160) and p53 (OMIM Ref. No. 191170), 2 proteins implicated in apoptosis and senescence. Ink4a/Arf deficiency rescued proliferation/senescence defects of Lig4-deficient fibroblasts but not other phenotypic aspects. In contrast, p53 deficiency rescued embryonic lethality, neuronal apoptosis, and fibroblast proliferation/senescence defects but not lymphocyte development or radiosensitivity. Young Lig4/p53 double-null mice routinely died from pro-B lymphomas. Thus, in the context of Lig4 deficiency, embryonic lethality and neuronal apoptosis likely result from a p53-dependent response to unrepaired DNA damage, and neuronal apoptosis and lymphocyte developmental defects can be mechanistically dissociated

[15144] It is appreciated that the abovementioned animal model for LIG4 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15145] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15146] Grawunder, U.; Zimmer, D.; Fugmann, S.; Schwarz, K.;

Lieber, M. R. : DNA ligase IV is essential for V(D)J recombination and DNA double-strand break repair in human precursor lymphocytes. Molec. Cell 2: 477-484, 1998. ; and

[15147] Frank, K. M.; Sekiguchi, J. M.; Seidl, K. J.; Swat, W.; Rathbun, G. A.; Cheng, H.-L.; Davidson, L.; Kangaloo, L.; Alt, F. W. : Late embryonic lethality and impaired V(D)J recombination in.

[15148] Further studies establishing the function and utilities of LIG4 are found in John Hopkins OMIM database record ID 601837, and in cited publications numbered 9053-9058, 887 and 8877 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM_018312) is another VGAM258 host target gene. C11orf23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C11orf23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C11orf23 BINDING SITE, designated SEQ ID:20300, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ

ID:2969.

[15149] Another function of VGAM258 is therefore inhibition of Chromosome 11 Open Reading Frame 23 (C11orf23, Accession NM_018312). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C11orf23. DKFZP434F0318 (Accession NM_030817) is another VGAM258 host target gene. DKFZP434F0318 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434F0318, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434F0318 BINDING SITE, designated SEQ ID:25141, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15150] Another function of VGAM258 is therefore inhibition of DKFZP434F0318 (Accession NM_030817). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434F0318. GFR (Accession NM_012294) is another VGAM258 host target gene. GFR BINDING SITE is

HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GFR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GFR BINDING SITE, designated SEQ ID:14638, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15151] Another function of VGAM258 is therefore inhibition of GFR (Accession NM_012294). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GFR. KIAA1301 (Accession XM_038999) is another VGAM258 host target gene. KIAA1301 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1301 BINDING SITE, designated SEQ ID:32975, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15152] Another function of VGAM258 is therefore inhibition of

KIAA1301 (Accession XM_038999). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1301. KIAA1922 (Accession XM_057040) is another VGAM258 host target gene. KIAA1922 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1922, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1922 BINDING SITE, designated SEQ ID:36453, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15153] Another function of VGAM258 is therefore inhibition of KIAA1922 (Accession XM_057040). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1922. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM_028840) is another VGAM258 host target gene. PPP1R16B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP1R16B, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R16B BINDING SITE, designated SEQ ID:30767, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15154] Another function of VGAM258 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 16B (PPP1R16B, Accession XM_028840). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R16B. PRO2958 (Accession NM_018546) is another VGAM258 host target gene. PRO2958 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO2958, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO2958 BINDING SITE, designated SEQ ID:20626, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15155] Another function of VGAM258 is therefore inhibition of PRO2958 (Accession NM_018546). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with PRO2958. LOC145725 (Accession XM_085211) is another VGAM258 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37950, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15156] Another function of VGAM258 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM258 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145732, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37959, to

the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15157] Another function of VGAM258 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC146540 (Accession XM_085497) is another VGAM258 host target gene. LOC146540 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146540 BINDING SITE, designated SEQ ID:38198, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15158] Another function of VGAM258 is therefore inhibition of LOC146540 (Accession XM_085497). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146540. LOC196957 (Accession XM_113789) is another VGAM258 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42431, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15159] Another function of VGAM258 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196957. LOC196961 (Accession XM_113790) is another VGAM258 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42440, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15160] Another function of VGAM258 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities

of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM258 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42458, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15161] Another function of VGAM258 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC199957 (Accession XM_114068) is another VGAM258 host target gene. LOC199957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC199957 BINDING SITE, designated SEQ ID:42672, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15162] Another function of VGAM258 is therefore inhibition of LOC199957 (Accession XM_114068). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199957. LOC256940 (Accession XM_172879) is another VGAM258 host target gene. LOC256940 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256940, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256940 BINDING SITE, designated SEQ ID:46154, to the nucleotide sequence of VGAM258 RNA, herein designated VGAM RNA, also designated SEQ ID:2969.

[15163] Another function of VGAM258 is therefore inhibition of LOC256940 (Accession XM_172879). Accordingly, utilities of VGAM258 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256940. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 259 (VGAM259) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15164] VGAM259 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM259 was detected is described hereinabove with reference to Figs. 1–8.

[15165] VGAM259 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15166] VGAM259 gene encodes a VGAM259 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM259 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM259 precursor RNA is designated SEQ ID:245, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:245 is located at position 56367 relative to the genome of Cal–

litrichine Herpesvirus 3.

[15167] VGAM259 precursor RNA folds onto itself, forming VGAM259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15168] An enzyme complex designated DICER COMPLEX, `dices` the VGAM259 folded precursor RNA into VGAM259 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM259 RNA is designated SEQ ID:2970, and is provided hereinbelow with reference to the sequence listing part.

[15169] VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM259 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15170] VGAM259 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM259 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM259 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15171] The complementary binding of VGAM259 RNA, herein designated VGAM RNA, to host target binding sites on VGAM259 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM259 host target RNA into VGAM259 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15172] It is appreciated that VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM259 host target genes. The mRNA of each one of this plurality of VGAM259 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM259 RNA, herein designated VGAM RNA, and which when bound by VGAM259 RNA causes inhibition of translation of respective one or more VGAM259 host target proteins.

[15173] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM259 gene, herein designated VGAM GENE, on one or more VGAM259 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15174] It is yet further appreciated that a function of VGAM259 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM259

correlate with, and may be deduced from, the identity of the host target genes which VGAM259 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [15175] Nucleotide sequences of the VGAM259 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM259 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM259 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM259 are further described hereinbelow with reference to Table 1.
- [15176] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM259 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM259 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [15177] As mentioned hereinabove with reference to Fig. 1, a function of VGAM259 gene, herein designated VGAM is inhibition of expression of VGAM259 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM259 correlate with, and may be deduced

from, the identity of the target genes which VGAM259 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15178] Amino-terminal Enhancer of Split (AES, Accession NM_001130) is a VGAM259 host target gene. AES BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AES, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AES BINDING SITE, designated SEQ ID:6803, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15179] A function of VGAM259 is therefore inhibition of Amino-terminal Enhancer of Split (AES, Accession NM_001130), a gene which may function during epithelial differentiation. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AES. The function of AES has been established by previous studies. In *Drosophila melanogaster*, neurogenesis is under the control of several loci whose products appear to determine the fate of neuroectodermal cells during embryonic development. One of these neuro-

genic loci is the enhancer of split gene complex. Hartley et al. (1988) serendipitously isolated a mouse cDNA which predicted a sequence of 202 amino acids exhibiting strong similarity with the amino-terminal region of *Drosophila* enhancer of split groucho protein. Miyasaka et al. (1993) reported the cDNA cloning, nucleotide and deduced amino acid sequencing, and tissue-specific expression of mouse and human AES (amino-terminal enhancer of split) and ESG (enhancer of split groucho) genes. (ESG is also called TLE for 'transducin-like enhancer of split.') Human AES transcripts of 1.6 kb and 1.4 kb were predominantly present in muscle, heart, and placenta. Using human/Chinese hamster hybrid cell lines, Miyasaka et al. (1993) mapped the human AES gene to chromosome 19. Hou and Li (1998) used fluorescence in situ hybridization to localize the AES gene to 19p13.3 near the transcription factor-3 (TCF3; 141741) gene. They also determined the nucleotide sequence for approximately 12 kb from the AES gene and showed that its protein-encoding sequence is interrupted by 6 introns.

[15180] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [15181] Hou, E. W.; Li, S.-L. : Genomic organization and chromosome localization to band 19p13.3 of the human AES gene: gene product exhibits strong similarity to the N-terminal domain of Drosophila enhancer of split Groucho protein. DNA Cell Biol. 17: 911-913, 1998. ; and
- [15182] Miyasaka, H.; Choudhury, B. K.; Hou, E. W.; Li, S. S.-L. : Molecular cloning and expression of mouse and human cDNA encoding AES and ESG proteins with strong similarity to Drosophila en.
- [15183] Further studies establishing the function and utilities of AES are found in John Hopkins OMIM database record ID 600188, and in cited publications numbered 10113-10115 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Contactin 2 (axonal) (CNTN2, Accession NM_005076) is another VGAM259 host target gene. CNTN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNTN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNTN2 BINDING SITE, designated SEQ ID:11523, to the nucleotide sequence of VGAM259 RNA, herein designated

VGAM RNA, also designated SEQ ID:2970.

[15184] Another function of VGAM259 is therefore inhibition of Contactin 2 (axonal) (CNTN2, Accession NM_005076), a gene which may play a role in axonal growth and cell adhesion. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNTN2. The function of CNTN2 has been established by previous studies. The pathfinding of axons toward their targets represents an early step in the development of the nervous system. Axonal extension involves selective interactions between molecules on the surface of the axon and those in the local microenvironment. Functional studies in vitro of axonal surface glycoproteins suggest that they are involved in cell adhesion and in the promotion of neurite outgrowth. One of these proteins, the rat transient axonal glycoprotein (Tag1), is expressed by restricted subsets of central and peripheral neurons during the initial phase of neurite outgrowth (Dodd et al., 1988). Tag1 belongs to the immunoglobulin superfamily. Tsiotra et al. (1993) isolated cDNAs encoding TAX1, the human homolog of TAG1. Human TAX1 showed a high degree of homology to the rat protein and less to its chick counterpart, axonin-1, with 91 and 75% identity

at the amino acid level, respectively. The numbers of immunoglobulin (IgC2) domains and fibronectin repeats present in TAG1 were conserved among the 3 species Rickman et al. (2001) found TAX1 to be amplified in 2 high-grade gliomas among a group of 26 gliomas investigated. Furthermore, they found high levels of TAX1 mRNA in glial tumors, even in the absence of TAX1 gene amplification. Because glial tumors are highly invasive and in view of the role of TAX1 in neurite outgrowth, they investigated the potential role of TAX1 in glioma cell migration. Using an in vitro assay, they found that the migration of glioma tumor cells is profoundly reduced in the presence of either an anti-TAX1 antibody or a TAX1 antisense oligonucleotide. The findings suggested that TAX1 plays a role in glial tumorigenesis and may provide a potential target for therapeutic intervention

[15185] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15186] Dodd, J.; Morton, S. B.; Karagogeos, D.; Yamamoto, M.; Jessell, T. M. : Spatial regulation of axonal glycoprotein expression on subsets of embryonic spinal neurons. *Neuron* 1: 105–116, 1988. ; and

[15187] Rickman, D. S.; Tyagi, R.; Zhu, X.-X.; Bobek, M. P.; Song, S.; Blaivas, M.; Misek, D. E.; Israel, M. A.; Kurnit, D. M.; Ross, D. A.; Kish, P. E.; Hanash, S. M. : The gene for the axonal.

[15188] Further studies establishing the function and utilities of CNTN2 are found in John Hopkins OMIM database record ID 190197, and in cited publications numbered 5741-574 and 5733-5734 listed in the bibliography section herein-below, which are also hereby incorporated by reference. Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990) is another VGAM259 host target gene. GABRE BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by GABRE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GABRE BINDING SITE, designated SEQ ID:22532, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15189] Another function of VGAM259 is therefore inhibition of Gamma-aminobutyric Acid (GABA) A Receptor, Epsilon (GABRE, Accession NM_021990), a gene which mediates

neuronal inhibition by binding to the gaba/ benzodiazepine receptor and opening an integral chloride channel. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GABRE. The function of GABRE has been established by previous studies. Davies et al. (1997) described a member of a new class of human GABA(A) receptor subunit, the epsilon subunit. The subunit was detected in the brain and can assemble with alpha and beta subunits. Wilke et al. (1997) also identified a cDNA sequence of a gene coding for a 506-amino acid protein, representing a member of a putative new class (epsilon) of the GABA-A receptor. The gene, symbolized GABRE, encodes a polypeptide almost identical to the one reported by Davies et al. (1997). GABRE was transcribed in several different tissues, with the highest levels being detected in adult heart and placenta. Wilke et al. (1997) observed alternative splicing of GABRE transcripts isolated from different tissues at multiple positions of the gene, yielding an unusually complex variety of cDNA variants. The structure of the 5-prime region of most cDNAs is compatible with expression of GABRE in adult brain only, whereas in other tissues, most transcripts code for trun-

cated protein sequences. The GABRE gene extends over 14 kb and is clustered together with the alpha-3 (OMIM Ref. No. 305660) and the putative beta-4 GABA-A receptor subunit genes in an interval of approximately 0.8 Mb in band Xq28. It is located in the candidate regions of 2 different neurologic diseases, early-onset parkinsonism, or Waisman syndrome (OMIM Ref. No. 311510), and MRX3 (OMIM Ref. No. 309541), a form of X-linked mental retardation. Sinkkonen et al. (2000) obtained cDNAs encoding rat Gabre and Gabrq (OMIM Ref. No. 300349), which are highly divergent from their human homologs. They noted that rat Gabre and Gabrq have expression patterns distinct from those reported in primates.

[15190] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15191] Davies, P. A.; Hanna, M. C.; Hales, T. G.; Kirkness, E. F. : Insensitivity to anaesthetic agents conferred by a class of GABA(A) receptor subunit. Nature 385: 820-823, 1997. ; and

[15192] Sinkkonen, S. T.; Hanna, M. C.; Kirkness, E. F.; Korpi, E. R. : GABA-A receptor epsilon and theta subunits display unusual structural variation between species and are en-

riched in the r.

[15193] Further studies establishing the function and utilities of GABRE are found in John Hopkins OMIM database record ID 300093, and in cited publications numbered 9081–9083 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. LENG4 (Accession NM_024298) is another VGAM259 host target gene. LENG4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LENG4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LENG4 BINDING SITE, designated SEQ ID:23578, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15194] Another function of VGAM259 is therefore inhibition of LENG4 (Accession NM_024298), a gene which may be a transmembrane protein. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LENG4. The function of LENG4 has been established by previous studies. Overexpression of genes is one of the genetic alterations

that may have a role in the development and progression of cancers. By immunoscreening a bladder tumor cell cDNA expression library with antibody to AN43, a bladder tumor-associated antigen, Fukunaga-Johnson et al. (1996) isolated a cDNA encoding BB1. The deduced 343-amino acid protein contains both hydrophilic and hydrophobic regions, suggesting that it may be a trans-membrane protein. Northern blot analysis revealed elevated expression of a 2.0-kb transcript in breast and bladder tumor cells compared with normal cells. Expression in the cancer cells could be reduced by treatment with gamma-interferon (IFNG; 147570). Because of a lack of reactivity of the expressed BB1 protein on Western blots, Fukunaga-Johnson et al. (1996) concluded that BB1 is distinct from the AN43 antigen. By genomic sequence analysis, Wende et al. (2000) mapped the BB1 gene, which they termed LENG4, to 19q13.4. They noted that the LENG genes, unlike other genes in the leukocyte receptor cluster on 19q13.4, do not encode proteins with immunoglobulin domains.

[15195] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15196] Fukunaga–Johnson, N.; Lee, S. W.; Liebert, M.; Grossman, H. B. : Molecular analysis of a gene, BB1, overexpressed in bladder and breast carcinoma. *Anticancer Res.* 16: 1085–1090, 1996. ; and

[15197] Wende, H.; Volz, A.; Ziegler, A. : Extensive gene duplications and a large inversion characterize the human leukocyte receptor cluster. *Immunogenetics* 51: 703–713, 2000.

[15198] Further studies establishing the function and utilities of LENG4 are found in John Hopkins OMIM database record ID 606048, and in cited publications numbered 6449 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Leucine–zipper–like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767) is another VGAM259 host target gene. LZTR1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LZTR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LZTR1 BINDING SITE, designated SEQ ID:13635, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15199] Another function of VGAM259 is therefore inhibition of Leucine–zipper–like Transcriptional Regulator, 1 (LZTR1, Accession NM_006767). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LZTR1. Neuroligin 2 (NLGN2, Accession XM_113932) is another VGAM259 host target gene. NLGN2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NLGN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NLGN2 BINDING SITE, designated SEQ ID:42548, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15200] Another function of VGAM259 is therefore inhibition of Neuroligin 2 (NLGN2, Accession XM_113932), a gene which rapidly hydrolyzes choline released into the synapse. Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NLGN2. The function of NLGN2 and its association with various diseases and clinical conditions, has been established by previous studies, as de–

scribed hereinabove with reference to VGAM178.Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945) is another VGAM259 host target gene. C21orf25 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C21orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf25 BINDING SITE, designated SEQ ID:31798, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15201] Another function of VGAM259 is therefore inhibition of Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf25. FLJ22814 (Accession NM_024916) is another VGAM259 host target gene. FLJ22814 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ22814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ22814 BINDING SITE, designated SEQ ID:24440, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15202] Another function of VGAM259 is therefore inhibition of FLJ22814 (Accession NM_024916). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22814. FLJ23519 (Accession NM_032240) is another VGAM259 host target gene. FLJ23519 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23519, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23519 BINDING SITE, designated SEQ ID:25974, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15203] Another function of VGAM259 is therefore inhibition of FLJ23519 (Accession NM_032240). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23519. HSGP25L2G (Accession XM_030771) is another VGAM259

host target gene. HSGP25L2G BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSGP25L2G, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSGP25L2G BINDING SITE, designated SEQ ID:31133, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15204] Another function of VGAM259 is therefore inhibition of HSGP25L2G (Accession XM_030771). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSGP25L2G. KIAA1257 (Accession XM_031577) is another VGAM259 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31437, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15205] Another function of VGAM259 is therefore inhibition of KIAA1257 (Accession XM_031577). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. MGC11352 (Accession XM_035941) is another VGAM259 host target gene. MGC11352 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC11352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC11352 BINDING SITE, designated SEQ ID:32353, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15206] Another function of VGAM259 is therefore inhibition of MGC11352 (Accession XM_035941). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC11352. MGC2721 (Accession NM_032737) is another VGAM259 host target gene. MGC2721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2721, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2721 BINDING SITE, designated SEQ ID:26461, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15207] Another function of VGAM259 is therefore inhibition of MGC2721 (Accession NM_032737). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2721. SSB-3 (Accession NM_080861) is another VGAM259 host target gene. SSB-3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSB-3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSB-3 BINDING SITE, designated SEQ ID:28099, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15208] Another function of VGAM259 is therefore inhibition of SSB-3 (Accession NM_080861). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSB-3.

TUSP (Accession NM_020245) is another VGAM259 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21531, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15209] Another function of VGAM259 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. LOC124987 (Accession XM_064384) is another VGAM259 host target gene. LOC124987 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC124987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124987 BINDING SITE, designated SEQ ID:37264, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA,

also designated SEQ ID:2970.

[15210] Another function of VGAM259 is therefore inhibition of LOC124987 (Accession XM_064384). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124987. LOC145725 (Accession XM_085211) is another VGAM259 host target gene. LOC145725 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145725, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145725 BINDING SITE, designated SEQ ID:37944, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15211] Another function of VGAM259 is therefore inhibition of LOC145725 (Accession XM_085211). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145725. LOC145732 (Accession XM_085218) is another VGAM259 host target gene. LOC145732 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145732, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145732 BINDING SITE, designated SEQ ID:37953, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15212] Another function of VGAM259 is therefore inhibition of LOC145732 (Accession XM_085218). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145732. LOC157918 (Accession XM_098842) is another VGAM259 host target gene. LOC157918 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC157918, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157918 BINDING SITE, designated SEQ ID:41892, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15213] Another function of VGAM259 is therefore inhibition of LOC157918 (Accession XM_098842). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC157918. LOC196957 (Accession XM_113789) is another VGAM259 host target gene. LOC196957 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196957 BINDING SITE, designated SEQ ID:42426, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15214] Another function of VGAM259 is therefore inhibition of LOC196957 (Accession XM_113789). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196957. LOC196961 (Accession XM_113790) is another VGAM259 host target gene. LOC196961 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC196961, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196961 BINDING SITE, designated SEQ ID:42435, to

the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15215] Another function of VGAM259 is therefore inhibition of LOC196961 (Accession XM_113790). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196961. LOC197138 (Accession XM_113829) is another VGAM259 host target gene. LOC197138 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197138, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197138 BINDING SITE, designated SEQ ID:42453, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15216] Another function of VGAM259 is therefore inhibition of LOC197138 (Accession XM_113829). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197138. LOC254439 (Accession XM_170659) is another VGAM259 host target gene. LOC254439 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC254439, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254439 BINDING SITE, designated SEQ ID:45433, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15217] Another function of VGAM259 is therefore inhibition of LOC254439 (Accession XM_170659). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254439. LOC255196 (Accession XM_173157) is another VGAM259 host target gene. LOC255196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC255196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255196 BINDING SITE, designated SEQ ID:46414, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15218] Another function of VGAM259 is therefore inhibition of LOC255196 (Accession XM_173157). Accordingly, utilities

of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255196. LOC257437 (Accession XM_166089) is another VGAM259 host target gene. LOC257437 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257437, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257437 BINDING SITE, designated SEQ ID:43854, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15219] Another function of VGAM259 is therefore inhibition of LOC257437 (Accession XM_166089). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257437. LOC90019 (Accession NM_138567) is another VGAM259 host target gene. LOC90019 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC90019, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90019 BINDING SITE, designated SEQ ID:28869, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15220] Another function of VGAM259 is therefore inhibition of LOC90019 (Accession NM_138567). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90019. LOC91496 (Accession XM_038788) is another VGAM259 host target gene. LOC91496 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91496, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91496 BINDING SITE, designated SEQ ID:32920, to the nucleotide sequence of VGAM259 RNA, herein designated VGAM RNA, also designated SEQ ID:2970.

[15221] Another function of VGAM259 is therefore inhibition of LOC91496 (Accession XM_038788). Accordingly, utilities of VGAM259 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91496. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 260 (VGAM260) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15222] VGAM260 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM260 was detected is described hereinabove with reference to Figs. 1–8.

[15223] VGAM260 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15224] VGAM260 gene encodes a VGAM260 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM260 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM260 precursor RNA is designated SEQ ID:246, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:246 is located at position 19614 relative to the genome of Cal–

litrichine Herpesvirus 3.

[15225] VGAM260 precursor RNA folds onto itself, forming VGAM260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15226] An enzyme complex designated DICER COMPLEX, `dices` the VGAM260 folded precursor RNA into VGAM260 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 85%) nucleotide sequence of VGAM260 RNA is designated SEQ ID:2971, and is provided hereinbelow with reference to the sequence listing part.

[15227] VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM260 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15228] VGAM260 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM260 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM260 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15229] The complementary binding of VGAM260 RNA, herein designated VGAM RNA, to host target binding sites on VGAM260 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM260 host target RNA into VGAM260 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15230] It is appreciated that VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM260 host target genes. The mRNA of each one of this plurality of VGAM260 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM260 RNA, herein designated VGAM RNA, and which when bound by VGAM260 RNA causes inhibition of translation of respective one or more VGAM260 host target proteins.

[15231] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM260 gene, herein designated VGAM GENE, on one or more VGAM260 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15232] It is yet further appreciated that a function of VGAM260 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM260

correlate with, and may be deduced from, the identity of the host target genes which VGAM260 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15233] Nucleotide sequences of the VGAM260 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM260 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM260 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM260 are further described hereinbelow with reference to Table 1.

[15234] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM260 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM260 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15235] As mentioned hereinabove with reference to Fig. 1, a function of VGAM260 gene, herein designated VGAM is inhibition of expression of VGAM260 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM260 correlate with, and may be deduced

from, the identity of the target genes which VGAM260 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15236] Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM_000644) is a VGAM260 host target gene. AGL BINDING SITE1 through AGL BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGL BINDING SITE1 through AGL BINDING SITE6, designated SEQ ID:6295, SEQ ID:6300, SEQ ID:6308, SEQ ID:5468, SEQ ID:6285 and SEQ ID:6290 respectively, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15237] A function of VGAM260 is therefore inhibition of Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM_000644). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGL.

Desmoglein 1 (DSG1, Accession NM_001942) is another VGAM260 host target gene. DSG1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DSG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DSG1 BINDING SITE, designated SEQ ID:7655, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15238] Another function of VGAM260 is therefore inhibition of Desmoglein 1 (DSG1, Accession NM_001942). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DSG1. Nerve Growth Factor Receptor (TNFRSF16) Associated Protein 1 (NGFRAP1, Accession NM_014380) is another VGAM260 host target gene. NGFRAP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NGFRAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NGFRAP1 BINDING SITE, designated SEQ ID:15716, to the

nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15239] Another function of VGAM260 is therefore inhibition of Nerve Growth Factor Receptor (TNFRSF16) Associated Protein 1 (NGFRAP1, Accession NM_014380), a gene which may play an important role in the pathogenesis of neuro-genetic diseases. Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NGFRAP1. The function of NGFRAP1 has been established by previous studies. The C-terminal cytoplasmic domain of p75(NTR) (NGFR; 162010) has a type-2 death domain. However, TRAF (e.g., TRAF6; 602355)-like proteins that interact with this domain do not affect NGF (OMIM Ref. No. 162030)-dependent apoptosis. Using a yeast 2-hybrid screen with the cytosolic domain of p75(NTR) as bait, Mukai et al. (2000) obtained cDNAs encoding mouse and human p75(NTR)-associated cell death executor, or NADE. Human NADE is identical to the HGR74 cDNA cloned by Rapp et al. (1990) from an ovarian granulosa cDNA library. HGR74 was expressed in testis, prostate, seminal vesicle, and ovarian granulosa cells (Rapp et al., 1990). By sequence analysis, Mukai et al. (2000) predicted that the

111-amino acid NADE protein has a leucine-rich nuclear export signal (NES) and 2 ubiquitination sequence boxes. Western blot analysis showed expression of mouse Nade only after proteasome inhibition, implying that native Nade is modified by the ubiquitin conjugating system. Immunofluorescence microscopy demonstrated expression of wildtype Nade, but not Nade carrying leu94-to-ala and leu97-to-ala mutations in the NES, in the cytoplasm. GST pull-down analysis indicated that the C terminus of Nade binds to the cytoplasmic cell death domain of p75(NTR). Coimmunoprecipitation analysis showed that NGF induces interaction of NADE and p75(NTR). TUNEL analysis determined that NGF, but not other neurotrophins, could induce apoptosis in cells expressing NADE and p75(NTR). NGF-treated cells expressing NADE and p75(NTR) processed CASP2 (OMIM Ref. No. 600639) and CASP3 (OMIM Ref. No. 600636) to their active forms. Confocal microscopy established that most NGF-treated oligodendrocytes underwent apoptosis and expressed NADE. Scott (2001) mapped the NGFRAP1 gene to Xq22.1-q23 based on sequence similarity between the NGFRAP1 sequence and the chromosome X clone RP13-349O20 (GenBank AL606763).

- [15240] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [15241] Mukai, J.; Hachiya, T.; Shoji-Hoshino, S.; Kimura, M. T.; Nadano, D.; Suvanto, P.; Hanaoka, T.; Li, Y.; Irie, S.; Greene, L. A.; Sato, T.-A. : NADE, a p75NTR-associated cell death executor, is involved in signal transduction mediated by the common neurotrophin receptor p75NTR. *J. Biol. Chem.* 275: 17566–17570, 2000. ; and
- [15242] Rapp, G.; Freudenstein, J.; Klaudiny, J.; Mucha, J.; Wempe, F.; Zimmer, M.; Scheit, K. H. : Characterization of three abundant mRNAs from human ovarian granulosa cells. *DNA Cell Biol.*
- [15243] Further studies establishing the function and utilities of NGFRAP1 are found in John Hopkins OMIM database record ID 300361, and in cited publications numbered 6731–6733 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Alpha Polypeptide I (P4HA1, Accession NM_000917) is another VGAM260 host target gene. P4HA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

P4HA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P4HA1 BINDING SITE, designated SEQ ID:6627, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15244] Another function of VGAM260 is therefore inhibition of Procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), Alpha Polypeptide I (P4HA1, Accession NM_000917), a gene which catalyzes the formation of 4-hydroxyproline in collagen. Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P4HA1. The function of P4HA1 has been established by previous studies. Prolyl 4-hydroxylase (EC 1.14.11.2) plays a central role in collagen synthesis. It catalyzes the formation of 4-hydroxyproline in collagens by hydroxylation of proline residues in peptide linkages. The 4-hydroxyproline residues are essential for the folding of the newly synthesized procollagen polypeptide chain into triple helical molecules. The active enzyme is a tetramer of 2 alpha and 2 beta subunits with a molecular weight of about

240,000. The beta subunit (P4HB; 176790) is identical to the enzyme disulfide isomerase (EC 5.3.4.1) and a major cellular thyroid-binding protein. The alpha subunit probably contributes a major part of the catalytic site of the enzyme. Helaakoski et al. (1989) isolated cDNA clones for the alpha subunit. They found that the clones encode a polypeptide of 517 amino acid residues and a signal peptide of 17 amino acids. Southern blot analyses of human genomic DNA with a cDNA probe for the alpha subunit suggested the presence of only 1 gene encoding 2 types of mRNA, which appear to result from mutually exclusive alternative splicing of primary transcripts of 1 gene.

Helaakoski et al. (1994) reported that the P4HA gene covers more than 69 kilobases and consists of 16 exons. Evidence had previously been presented for a mutually exclusive alternative splicing of RNA transcripts of the gene. The present data indicated that the mutually exclusive sequences found in the mRNAs are coded by 2 consecutive, homologous 71-bp exons, 9 and 10. These exons are identical in their first 5 basepairs and the overall identity between them is 61% at the nucleotide level and 58% at the level of the coded amino acids. Both types of mRNA were found to be expressed in all of the tissues studied,

but in some tissues the type coding for the exon 9 or exon 10 sequences was more abundant than the other type.

[15245] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15246] Helaakoski, T.; Vuori, K.; Myllyla, R.; Kivirikko, K. I.; Pihlajaniemi, T. : Molecular cloning of the alpha-subunit of human prolyl 4-hydroxylase: the complete cDNA-derived amino acid sequence and evidence for alternative splicing of RNA transcripts. Proc. Nat. Acad. Sci. 86: 4392-4396, 1989. ; and

[15247] Helaakoski, T.; Veijola, J.; Vuori, K.; Rehn, M.; Chow, L. T.; Taillon-Miller, P.; Kivirikko, K. I.; Pihlajaniemi, T. : Structure and expression of the human gene for the alpha subunit.

[15248] Further studies establishing the function and utilities of P4HA1 are found in John Hopkins OMIM database record ID 176710, and in cited publications numbered 1523-152 and 1528-1527 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069) is another VGAM260

host target gene. ATP1B4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B4 BINDING SITE, designated SEQ ID:14329, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15249] Another function of VGAM260 is therefore inhibition of ATPase, (Na⁺)/K⁺ Transporting, Beta 4 Polypeptide (ATP1B4, Accession NM_012069). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B4. KIAA1209 (Accession XM_027307) is another VGAM260 host target gene. KIAA1209 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1209, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1209 BINDING SITE, designated SEQ ID:30475, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2971.

[15250] Another function of VGAM260 is therefore inhibition of KIAA1209 (Accession XM_027307). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1209. MGC15482 (Accession NM_032875) is another VGAM260 host target gene. MGC15482 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC15482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15482 BINDING SITE, designated SEQ ID:26696, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15251] Another function of VGAM260 is therefore inhibition of MGC15482 (Accession NM_032875). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15482. LOC130733 (Accession XM_059466) is another VGAM260 host target gene. LOC130733 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130733, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130733 BINDING SITE, designated SEQ ID:37004, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15252] Another function of VGAM260 is therefore inhibition of LOC130733 (Accession XM_059466). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130733. LOC152059 (Accession XM_087372) is another VGAM260 host target gene. LOC152059 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152059, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152059 BINDING SITE, designated SEQ ID:39210, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15253] Another function of VGAM260 is therefore inhibition of LOC152059 (Accession XM_087372). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC152059. LOC154743 (Accession XM_088029) is another VGAM260 host target gene. LOC154743 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154743, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154743 BINDING SITE, designated SEQ ID:39480, to the nucleotide sequence of VGAM260 RNA, herein designated VGAM RNA, also designated SEQ ID:2971.

[15254] Another function of VGAM260 is therefore inhibition of LOC154743 (Accession XM_088029). Accordingly, utilities of VGAM260 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154743. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 261 (VGAM261) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15255] VGAM261 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM261 was detected is described hereinabove with reference to Figs. 1–8.

[15256] VGAM261 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15257] VGAM261 gene encodes a VGAM261 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM261 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM261 precursor RNA is designated SEQ ID:247, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:247 is located at position 117465 relative to the genome of Callitrichine Herpesvirus 3.

[15258] VGAM261 precursor RNA folds onto itself, forming VGAM261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15259] An enzyme complex designated DICER COMPLEX, `dices` the VGAM261 folded precursor RNA into VGAM261 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 54%) nucleotide sequence of VGAM261 RNA is designated SEQ ID:2972, and is provided hereinbelow with reference to the sequence listing part.

[15260] VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM261 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15261] VGAM261 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM261 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM261 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15262] The complementary binding of VGAM261 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM261 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM261 host target RNA into VGAM261 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15263] It is appreciated that VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM261 host target genes. The mRNA of each one of this plurality of VGAM261 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM261 RNA, herein designated VGAM RNA, and which when bound by VGAM261 RNA causes inhibition of translation of respective one or more VGAM261 host target proteins.

[15264] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM261 gene, herein designated VGAM GENE, on one or more VGAM261 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15265] It is yet further appreciated that a function of VGAM261 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM261 correlate with, and may be deduced from, the identity of the host target genes which VGAM261 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15266] Nucleotide sequences of the VGAM261 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM261 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM261 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM261 are further described hereinbelow with reference to Table 1.

[15267] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM261 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM261 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15268] As mentioned hereinabove with reference to Fig. 1, a function of VGAM261 gene, herein designated VGAM is inhibition of expression of VGAM261 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM261 correlate with, and may be deduced from, the identity of the target genes which VGAM261 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15269] Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350) is a VGAM261 host target gene. PDGFRB BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by PDGFRB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDGFRB BINDING SITE, designated SEQ ID:32813, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15270] A function of VGAM261 is therefore inhibition of Platelet-derived Growth Factor Receptor, Beta Polypeptide (PDGFRB, Accession XM_038350), a gene which Platelet-derived growth factor receptor beta chain; tyrosine kinase receptor. Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDGFRB. The function of PDGFRB and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM125. Promyelocytic Leukemia (PML, Accession NM_033238) is another VGAM261 host target gene. PML BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PML, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE, designated SEQ ID:27076, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15271] Another function of VGAM261 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM_033238). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PML. Pleckstrin and Sec7 Domain Protein (PSD, Accession NM_002779) is another VGAM261 host target gene. PSD BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PSD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PSD BINDING SITE, designated SEQ ID:8668, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15272] Another function of VGAM261 is therefore inhibition of Pleckstrin and Sec7 Domain Protein (PSD, Accession NM_002779), a gene which promotes guanine-nucleotide exchange on arf6. Accordingly, utilities of VGAM261 in-

clude diagnosis, prevention and treatment of diseases and clinical conditions associated with PSD. The function of PSD has been established by previous studies. Perletti et al. (1997) identified a novel human gene on 10q24, contiguous to the 3-prime end of the NFKB2 gene (OMIM Ref. No. 164012) in a tail-to-tail arrangement. They described a cDNA of 4,307 bp, isolated from an adult human brain cDNA library, which contains an open reading frame encoding a putative protein of 645 amino acids with a predicted molecular weight of 71 kD. Database homology searches indicated that the novel gene codes for a putative protein containing 2 discrete domains with significant homology to the Sec7 and pleckstrin-homology (PH) domains, respectively. They used the gene symbol PSD for 'pleckstrin-Sec7 domains.' Northern blot analysis of a panel of RNAs from normal human tissues using the PSD cDNA as probe revealed the presence of 3 different tissue-specific transcripts of approximately 4.3, 2.3, and 1.8 kb, the longest of which was expressed only in brain. The data suggested that the PSD gene may encode a protein related to the protein family containing both the Sec7 in the PH domains and thought to be involved in signaling transduction processes. Other human proteins in the

same family include cytohesin-1 (Kolanus et al., 1996) and ARNO (OMIM Ref. No. 602488) (Chardin et al., 1996).

[15273] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15274] Kolanus, W.; Nagel, W.; Schiller, B.; Zeitlmann, L.; Godar, S.; Stockinger, H.; Seed, B. : Alpha-L-beta-2 integrin/ LFA-1 binding to ICAM-1 induced by cytohesin-1, a cytoplasmic regulatory molecule. Cell 86: 233-242, 1996. ; and

[15275] Perletti, L.; Talarico, D.; Trecca, D.; Ronchetti, D.; Fracchiolla, N. S.; Maiolo, A. T.; Neri, A. : Identification of a novel gene, PSD, adjacent to NFkB2/lyt-10, which contains Sec7 an.

[15276] Further studies establishing the function and utilities of PSD are found in John Hopkins OMIM database record ID 602327, and in cited publications numbered 600 and 10704 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155) is another VGAM261 host target gene. SERPINB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SERPINB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB9 BINDING SITE, designated SEQ ID:10364, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15277] Another function of VGAM261 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155), a gene which may be a serpin serine protease inhibitor that interacts with granzyme B (GZMB). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB9. The function of SERPINB9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60. Src-like-adaptor 2 (SLA2, Accession NM_032214) is another VGAM261 host target gene. SLA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SLA2 BINDING SITE, designated SEQ ID:25941, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15278] Another function of VGAM261 is therefore inhibition of Src-like-adaptor 2 (SLA2, Accession NM_032214). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLA2. Apolipoprotein L, 3 (APOL3, Accession NM_014349) is another VGAM261 host target gene.

APOL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL3 BINDING SITE, designated SEQ ID:15674, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15279] Another function of VGAM261 is therefore inhibition of Apolipoprotein L, 3 (APOL3, Accession NM_014349). Accordingly, utilities of VGAM261 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with APOL3. ERAP140 (Accession XM_059748) is another VGAM261 host target gene. ERAP140 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERAP140, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERAP140 BINDING SITE, designated SEQ ID:37084, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15280] Another function of VGAM261 is therefore inhibition of ERAP140 (Accession XM_059748). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERAP140. IKKE (Accession NM_014002) is another VGAM261 host target gene. IKKE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IKKE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IKKE BINDING SITE, designated SEQ ID:15201, to the nucleotide sequence of VGAM261 RNA,

herein designated VGAM RNA, also designated SEQ ID:2972.

[15281] Another function of VGAM261 is therefore inhibition of IKKE (Accession NM_014002). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IKKE. LOC127534 (Accession XM_060532) is another VGAM261 host target gene. LOC127534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC127534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC127534 BINDING SITE, designated SEQ ID:37168, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15282] Another function of VGAM261 is therefore inhibition of LOC127534 (Accession XM_060532). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC127534. LOC145082 (Accession XM_096719) is another VGAM261 host target gene. LOC145082 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145082 BINDING SITE, designated SEQ ID:40492, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15283] Another function of VGAM261 is therefore inhibition of LOC145082 (Accession XM_096719). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145082. LOC170082 (Accession XM_093092) is another VGAM261 host target gene. LOC170082 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC170082, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC170082 BINDING SITE, designated SEQ ID:40169, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15284] Another function of VGAM261 is therefore inhibition of LOC170082 (Accession XM_093092). Accordingly, utilities

of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC170082. LOC220370 (Accession XM_166943) is another VGAM261 host target gene. LOC220370 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220370, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220370 BINDING SITE, designated SEQ ID:44598, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15285] Another function of VGAM261 is therefore inhibition of LOC220370 (Accession XM_166943). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220370. LOC221540 (Accession XM_168133) is another VGAM261 host target gene. LOC221540 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221540, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221540 BINDING SITE, designated SEQ ID:45043, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15286] Another function of VGAM261 is therefore inhibition of LOC221540 (Accession XM_168133). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221540. LOC257545 (Accession XM_175217) is another VGAM261 host target gene. LOC257545 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257545, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257545 BINDING SITE, designated SEQ ID:46691, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15287] Another function of VGAM261 is therefore inhibition of LOC257545 (Accession XM_175217). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257545. LOC257598 (Accession XM_175295) is another VGAM261 host target gene. LOC257598 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257598, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257598 BINDING SITE, designated SEQ ID:46748, to the nucleotide sequence of VGAM261 RNA, herein designated VGAM RNA, also designated SEQ ID:2972.

[15288] Another function of VGAM261 is therefore inhibition of LOC257598 (Accession XM_175295). Accordingly, utilities of VGAM261 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257598. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 262 (VGAM262) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15289] VGAM262 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM262 was detected is described hereinabove with reference to Figs. 1-8.

[15290] VGAM262 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15291] VGAM262 gene encodes a VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM262 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM262 precursor RNA is designated SEQ ID:248, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:248 is located at position 13862 relative to the genome of Callitrichine Herpesvirus 3.

[15292] VGAM262 precursor RNA folds onto itself, forming VGAM262 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[15293] An enzyme complex designated DICER COMPLEX, `dices` the VGAM262 folded precursor RNA into VGAM262 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM262 RNA is designated SEQ ID:2973, and is provided hereinbelow with reference to the sequence listing part.

[15294] VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM262 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15295] VGAM262 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM262 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM262 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM262 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15296] The complementary binding of VGAM262 RNA, herein designated VGAM RNA, to host target binding sites on VGAM262 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM262 host target RNA into VGAM262 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15297] It is appreciated that VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM262 host target genes. The mRNA of each one of this plurality of VGAM262 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM262 RNA, herein designated VGAM RNA, and which when bound by VGAM262 RNA causes inhibition of translation of respective one or more VGAM262 host target proteins.

[15298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM262 gene, herein designated VGAM GENE, on one or more VGAM262 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15299] It is yet further appreciated that a function of VGAM262 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM262 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM262 correlate with, and may be deduced from, the identity of the host target genes which VGAM262 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15300] Nucleotide sequences of the VGAM262 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM262 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM262 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM262 are further described hereinbelow with reference to Table 1.

[15301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM262 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM262 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15302] As mentioned hereinabove with reference to Fig. 1, a function of VGAM262 gene, herein designated VGAM is inhibition of expression of VGAM262 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM262 correlate with, and may be deduced from, the identity of the target genes which VGAM262 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15303] FLJ21432 (Accession NM_024551) is a VGAM262 host target gene. FLJ21432 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21432, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21432 BINDING SITE, designated SEQ ID:23765, to the nucleotide sequence of VGAM262

RNA, herein designated VGAM RNA, also designated SEQ ID:2973.

[15304] A function of VGAM262 is therefore inhibition of FLJ21432 (Accession NM_024551). Accordingly, utilities of VGAM262 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21432. LOC204010 (Accession XM_115138) is another VGAM262 host target gene. LOC204010 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204010, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204010 BINDING SITE, designated SEQ ID:43081, to the nucleotide sequence of VGAM262 RNA, herein designated VGAM RNA, also designated SEQ ID:2973.

[15305] Another function of VGAM262 is therefore inhibition of LOC204010 (Accession XM_115138). Accordingly, utilities of VGAM262 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204010. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 263 (VGAM263) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15306] VGAM263 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM263 was detected is described hereinabove with reference to Figs. 1–8.

[15307] VGAM263 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15308] VGAM263 gene encodes a VGAM263 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM263 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM263 precursor RNA is designated SEQ ID:249, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:249 is located at position 131570 relative to the genome of Callitrichine Herpesvirus 3.

[15309] VGAM263 precursor RNA folds onto itself, forming VGAM263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15310] An enzyme complex designated DICER COMPLEX, `dices` the VGAM263 folded precursor RNA into VGAM263 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM263 RNA is designated SEQ ID:2974, and is provided hereinbelow with reference to the sequence listing part.

[15311] VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM263 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM263 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15312] VGAM263 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM263 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM263 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15313] The complementary binding of VGAM263 RNA, herein designated VGAM RNA, to host target binding sites on VGAM263 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM263 host target RNA into VGAM263 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15314] It is appreciated that VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM263 host target genes. The mRNA of each one of this plurality of VGAM263 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM263 RNA, herein designated VGAM RNA, and which when bound by VGAM263 RNA causes inhibition of translation of respective one or more VGAM263 host target proteins.

[15315] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM263 gene, herein designated VGAM GENE, on one or more VGAM263 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15316] It is yet further appreciated that a function of VGAM263 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM263 correlate with, and may be deduced from, the identity of

the host target genes which VGAM263 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [15317] Nucleotide sequences of the VGAM263 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM263 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM263 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM263 are further described hereinbelow with reference to Table 1.
- [15318] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM263 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM263 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [15319] As mentioned hereinabove with reference to Fig. 1, a function of VGAM263 gene, herein designated VGAM is inhibition of expression of VGAM263 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM263 correlate with, and may be deduced from, the identity of the target genes which VGAM263

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15320] Histone Deacetylase 5 (HDAC5, Accession NM_139205) is a VGAM263 host target gene. HDAC5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HDAC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HDAC5 BINDING SITE, designated SEQ ID:29221, to the nucleotide sequence of VGAM263 RNA, herein designated VGAM RNA, also designated SEQ ID:2974.

[15321] A function of VGAM263 is therefore inhibition of Histone Deacetylase 5 (HDAC5, Accession NM_139205), a gene which is responsible for the deacetylation of lysine residues on the n-terminal part of the core histones and mediate transcriptional regulation. Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HDAC5. The function of HDAC5 has been established by previous studies. Members of the myocyte enhancer factor-2 (MEF2A; 600660) family of transcription factors associate with myogenic basic helix-loop-helix transcription factors

such as MYOD1 (OMIM Ref. No. 159970) to activate skeletal myogenesis. MEF2 proteins also interact with the class II histone deacetylases HDAC4 and HDAC5, resulting in repression of MEF2-dependent genes. Execution of the muscle differentiation program requires release of MEF2 from repression by HDACs, which are expressed constitutively in myoblasts and myotubes. McKinsey et al. (2000) demonstrated that HDAC5 shuttles from the nucleus to the cytoplasm when myoblasts are triggered to differentiate. Calcium/calmodulin-dependent protein kinase (CAMK1; 604998) signaling, which stimulates myogenesis and prevents formation of MEF2-HDAC complexes, also induces nuclear export of HDAC4 and HDAC5 by phosphorylation of these transcriptional repressors. An HDAC5 mutant lacking 2 CAMK phosphorylation sites is resistant to CAMK-mediated nuclear export and acts as a dominant inhibitor of skeletal myogenesis, whereas a cytoplasmic HDAC5 mutant is unable to block efficiently the muscle differentiation program. McKinsey et al. (2000) concluded that their results highlight a mechanism for transcriptional regulation through signal and differentiation-dependent nuclear export of a chromatin-remodeling enzyme, and suggest that nucleocytoplasmic trafficking of HDACs is in-

volved in the control of cellular differentiation. Nagase et al. (1998) isolated a partial cDNA encoding HDAC5, which they called KIAA0600, from a brain cDNA library. RT-PCR analysis detected HDAC5 expression in all tissues tested, with relatively low expression in spleen and pancreas. By serologic analysis of recombinant colon cancer cDNA expression libraries, Scanlan et al. (1998) identified a partial cDNA encoding HDAC5, which they called NYCO9. Northern blot and RT-PCR analysis indicated weak but universal expression of a 3.7-kb HDAC5 transcript. Serologic analysis demonstrated that 5 of 29 colon cancer patients had antibodies to HDAC5.

[15322] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15323] Nagase, T.; Ishikawa, K.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. IX. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro. DNA Res. 5: 31-39, 1998. ; and

[15324] McKinsey, T. A.; Zhang, C.-L.; Lu, J.; Olson, E. N. : Signal-dependent nuclear export of a histone deacetylase regu-

lates muscle differentiation. Nature 408: 106–111, 2000.

[15325] Further studies establishing the function and utilities of HDAC5 are found in John Hopkins OMIM database record ID 605315, and in cited publications numbered 10820–448 and 6735 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275) is another VGAM263 host target gene. IL1F5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1F5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1F5 BINDING SITE, designated SEQ ID:14595, to the nucleotide sequence of VGAM263 RNA, herein designated VGAM RNA, also designated SEQ ID:2974.

[15326] Another function of VGAM263 is therefore inhibition of Interleukin 1 Family, Member 5 (delta) (IL1F5, Accession NM_012275), a gene which is a novel interleukin-1 receptor antagonist gene. Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL1F5. The function of IL1F5 has been established by previous studies. The cy-

tokine interleukin-1 (IL1; OMIM Ref. No. 147760) elicits a wide array of biologic activities that initiate and promote the host response to injury or infection by activating a set of transcription factors, including NFkB (see OMIM Ref. No. 164011) and AP1 (see OMIM Ref. No. 165160), which in turn induce production of effectors of the inflammatory response. Using a high-throughput cDNA screening technology and BLAST searching, followed by additional library screenings, RT-PCR, and 5-prime RACE analysis, Mulero et al. (1999) isolated a cDNA encoding a novel member of the interleukin-1 family, which they termed IL1HY1. The deduced 155-amino acid protein shares 52% sequence identity with IL1RA (OMIM Ref. No. 147679). It contains 3 of 4 highly conserved cysteine residues and an aspartate at position 148, which is cognate to asp145 in IL1B (OMIM Ref. No. 147720), and has been shown to impart agonist activity to IL1B. It does not contain a signal peptide or a prodomain. PCR analysis revealed expression in leukocytes, spleen, and brain as well as in fetal brain and most abundantly in a fetal skin library. RT-PCR analysis also established that IL1HY1 expression is amplified in a stimulated macrophage cell line. By EST database searching, Smith et al. (2000) also identified a cDNA encoding

IL1HY1, which they termed FIL1–delta. Modeling indicated that IL1HY1 has a conserved 12–stranded beta–trefoil structure. Binding analysis detected no interaction with multiple IL1R family members.

[15327] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15328] Busfield, S. J.; Comrack, C. A.; Yu, G.; Chickering, T. W.; Smutko, J. S.; Zhou, H.; Leiby, K. R.; Holmgren, L. M.; Gearing, D. P.; Pan, Y. : Identification and gene organization of three novel members of the IL–1 family on human chromosome 2. *Genomics* 66: 213–216, 2000. ; and

[15329] Mulero, J. J.; Pace, A. M.; Nelken, S. T.; Loeb, D. B.; Correa, T. R.; Drmanac, R.; Ford, J. E. : IL1HY1: a novel interleukin–1 receptor antagonist gene. *Biochem. Biophys. Res. Commun.*

[15330] Further studies establishing the function and utilities of IL1F5 are found in John Hopkins OMIM database record ID 605507, and in cited publications numbered 4500–450 and 4493 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155) is another

VGAM263 host target gene. SERPINB9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERPINB9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERPINB9 BINDING SITE, designated SEQ ID:10360, to the nucleotide sequence of VGAM263 RNA, herein designated VGAM RNA, also designated SEQ ID:2974.

[15331] Another function of VGAM263 is therefore inhibition of Serine (or cysteine) Proteinase Inhibitor, Clade B (ovalbumin), Member 9 (SERPINB9, Accession NM_004155), a gene which may be a serpin serine protease inhibitor that interacts with granzyme B (GZMB). Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERPINB9. The function of SERPINB9 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM60.RI58 (Accession NM_012420) is another VGAM263 host target gene. RI58 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RI58, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RI58 BINDING SITE, designated SEQ ID:14792, to the nucleotide sequence of VGAM263 RNA, herein designated VGAM RNA, also designated SEQ ID:2974.

[15332] Another function of VGAM263 is therefore inhibition of RI58 (Accession NM_012420). Accordingly, utilities of VGAM263 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RI58. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 264 (VGAM264) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15333] VGAM264 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM264 was detected is described hereinabove with reference to Figs. 1–8.

[15334] VGAM264 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM264 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[15335] VGAM264 gene encodes a VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM264 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM264 precursor RNA is designated SEQ ID:250, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:250 is located at position 45887 relative to the genome of Calitrichine Herpesvirus 3.

[15336] VGAM264 precursor RNA folds onto itself, forming VGAM264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15337] An enzyme complex designated DICER COMPLEX, `dices` the VGAM264 folded precursor RNA into VGAM264 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM264 RNA is designated SEQ ID:2975, and is provided hereinbelow with reference to the sequence listing part.

[15338] VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM264 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15339] VGAM264 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM264 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM264 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15340] The complementary binding of VGAM264 RNA, herein designated VGAM RNA, to host target binding sites on VGAM264 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM264 host target RNA into VGAM264 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[15341] It is appreciated that VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM264 host target genes. The mRNA of each one of this plurality of VGAM264 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM264 RNA, herein designated VGAM RNA, and which when bound by VGAM264 RNA causes inhibition of translation of respective one or more VGAM264 host target proteins.

[15342] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM264 gene, herein designated VGAM GENE, on one or more VGAM264 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15343] It is yet further appreciated that a function of VGAM264 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM264 correlate with, and may be deduced from, the identity of the host target genes which VGAM264 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15344] Nucleotide sequences of the VGAM264 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM264 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM264 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM264 are further described hereinbelow with reference to Table 1.

[15345] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM264 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM264 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15346] As mentioned hereinabove with reference to Fig. 1, a function of VGAM264 gene, herein designated VGAM is inhibition of expression of VGAM264 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM264 correlate with, and may be deduced from, the identity of the target genes which VGAM264 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15347] A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis factor, alpha, converting enzyme) (ADAM17, Accession NM_003183) is a VGAM264 host target gene. ADAM17 BINDING SITE1 and ADAM17 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAM17, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAM17 BIND-

ING SITE1 and ADAM17 BINDING SITE2, designated SEQ ID:9156 and SEQ ID:22409 respectively, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15348] A function of VGAM264 is therefore inhibition of A Disintegrin and Metalloproteinase Domain 17 (tumor necrosis factor, alpha, converting enzyme) (ADAM17, Accession NM_003183), a gene which member of ADAM family of zinc metalloproteases. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAM17. The function of ADAM17 has been established by previous studies. Black et al. (1997) cloned a human cDNA encoding ADAM17, which they called TACE. The gene encodes an 824-amino acid polypeptide containing the features of the ADAM family: a secretory signal sequence, a disintegrin domain, and a metalloprotease domain. Expression studies showed that the encoded protein cleaves precursor tumor necrosis factor-alpha (TNFA; 191160) to its mature form. Northern blot analysis revealed that the gene was expressed as a 5-kb mRNA in all tissues examined. Black et al. (1997) generated mouse T cells with a homozygous deficiency in the TACE gene; these cells

showed an 80 to 90% reduction in the release of TNFA. Yamazaki et al. (1998) used PCR of a backcross panel to map the mouse Tace gene to the proximal arm of chromosome 12. Hirohata et al. (1998) used radiation hybrids to map ADAM17 to human chromosome 2p25. Animal model experiments lend further support to the function of ADAM17. Peschon et al. (1998) found that mice lacking the zinc-binding domain of Tace died in utero after embryonic day 17.5 or failed to survive beyond 1 week of age.

[15349] It is appreciated that the abovementioned animal model for ADAM17 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15350] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15351] Black, R. A.; Rauch, C. T.; Kozlosky, C. J.; Peschon, J. J.; Slack, J. L.; Wolfson, M. F.; Castner, B. J.; Stocking, K. L.; Reddy, P.; Srinivasan, S.; Nelson, N.; Boiani, N.; Schooley, K. A.; Gerhart, M.; Davis, R.; Fitzner, J. N.; Johnson, R. S.; Paxton, R. J.; March, C. J.; Cerretti, D. P. : A metalloproteinase disintegrin that releases tumour-necrosis factor-

alpha from cells. Nature 385: 729–733, 1997. ; and

[15352] Peschon, J. J.; Slack, J. L.; Reddy, P.; Stocking, K. L.; Sunnarborg, S. W.; Lee, D. C.; Russell, W. E.; Castner, B. J.; Johnson, R. S.; Fitzner, J. N.; Boyce, R. W.; Nelson, N.; Kozlosk.

[15353] Further studies establishing the function and utilities of ADAM17 are found in John Hopkins OMIM database record ID 603639, and in cited publications numbered 7990, 7991–7992, 276 and 7993–7995 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 2, Regulatory Subunit B (B56), Beta Isoform (PPP2R5B, Accession NM_006244) is another VGAM264 host target gene. PPP2R5B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP2R5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5B BINDING SITE, designated SEQ ID:12915, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15354] Another function of VGAM264 is therefore inhibition of

Protein Phosphatase 2, Regulatory Subunit B (B56), Beta Isoform (PPP2R5B, Accession NM_006244), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP2R5B. The function of PPP2R5B has been established by previous studies. Protein phosphorylation is a regulatory mechanism commonly employed in cellular processes such as cell cycle progression, growth factor signaling, and cell transformation. Protein phosphatase 2A (PP2A), a heterotrimeric serine/threonine phosphatase, has been implicated in a variety of regulatory processes including cell growth and division, muscle contraction, and gene transcription. PP2A is a trimeric enzyme composed of a catalytic subunit (OMIM Ref. No. 176915), a structural subunit, and any of several different regulatory subunits which control its specificity. One family of related PP2A regulatory subunits is designated the B56 family and contains at least 5 different members (McCright and Virshup (1995)). The beta, delta (OMIM Ref. No. 601646), and epsilon (OMIM Ref. No. 601647) subunits are expressed at highest levels in the brain and the expression of the beta and delta subunits increases when

neuroblastoma cells are induced to differentiate with retinoic acid. See also the alpha subunit (OMIM Ref. No. 601643). McCright et al. (1996) mapped the gene for the beta subunit, designated PPP2R5B, to 11q12 by fluorescence in situ hybridization. The European Consortium on MEN1 (1997) localized the PPP2R5B gene to 11q13 in the course of constructing a contig of the region containing the MEN1 gene (OMIM Ref. No. 131100).

[15355] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15356] McCright, B.; Brothman, A. R.; Virshup, D. M. : Assignment of human protein phosphatase 2A regulatory subunit genes B56-alpha, B56-beta, B56-gamma, B56-delta, and B56-epsilon (PPP2R5A--PPP2R5E), highly expressed in muscle and brain, to chromosome regions 1q41, 11q12, 3p21, 6p21.1, and 7p11.2-to-p12. Genomics 36: 168-170, 1996. ; and

[15357] McCright, B.; Virshup, D. M. : Identification of a new family of protein phosphatase 2A regulatory subunits. J. Biol. Chem. 270: 26123-26128, 1995.

[15358] Further studies establishing the function and utilities of PPP2R5B are found in John Hopkins OMIM database record

ID 601644, and in cited publications numbered 648 and 6687–6688 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM_012102) is another VGAM264 host target gene. RERE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RERE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RERE BINDING SITE, designated SEQ ID:14410, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15359] Another function of VGAM264 is therefore inhibition of Arginine–glutamic Acid Dipeptide (RE) Repeats (RERE, Accession NM_012102), a gene which binds DRPLA and locates in the nucleus. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RERE. The function of RERE and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM51. Sodium Channel, Voltage–gated, Type IV, Alpha Polypeptide

(SCN4A, Accession NM_000334) is another VGAM264 host target gene. SCN4A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SCN4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCN4A BINDING SITE, designated SEQ ID:5890, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15360] Another function of VGAM264 is therefore inhibition of Sodium Channel, Voltage-gated, Type IV, Alpha Polypeptide (SCN4A, Accession NM_000334). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCN4A. Thrombospondin 1 (THBS1, Accession NM_003246) is another VGAM264 host target gene. THBS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by THBS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of THBS1 BINDING SITE, designated SEQ ID:9256, to the nucleotide se-

quence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15361] Another function of VGAM264 is therefore inhibition of Thrombospondin 1 (THBS1, Accession NM_003246), a gene which is a member of a family of adhesive molecules, involves in blood clotting and in angiogenesis. Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with THBS1. The function of THBS1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM20. Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575) is another VGAM264 host target gene. C17orf31 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C17orf31, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C17orf31 BINDING SITE, designated SEQ ID:18998, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15362] Another function of VGAM264 is therefore inhibition of

Chromosome 17 Open Reading Frame 31 (C17orf31, Accession NM_017575). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C17orf31. CGI-96 (Accession NM_015703) is another VGAM264 host target gene. CGI-96 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CGI-96, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-96 BINDING SITE, designated SEQ ID:17926, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15363] Another function of VGAM264 is therefore inhibition of CGI-96 (Accession NM_015703). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-96. DRIL2 (Accession NM_006465) is another VGAM264 host target gene. DRIL2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRIL2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of DRIL2 BINDING SITE, designated SEQ ID:13184, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15364] Another function of VGAM264 is therefore inhibition of DRIL2 (Accession NM_006465). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRIL2. FLJ14957 (Accession NM_032866) is another VGAM264 host target gene. FLJ14957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14957 BINDING SITE, designated SEQ ID:26680, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15365] Another function of VGAM264 is therefore inhibition of FLJ14957 (Accession NM_032866). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14957.

KIAA1056 (Accession NM_014894) is another VGAM264 host target gene. KIAA1056 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1056, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1056 BINDING SITE, designated SEQ ID:17050, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15366] Another function of VGAM264 is therefore inhibition of KIAA1056 (Accession NM_014894). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1056. KIAA1323 (Accession XM_032146) is another VGAM264 host target gene. KIAA1323 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1323 BINDING SITE, designated SEQ ID:31567, to the nucleotide sequence of VGAM264 RNA, herein designated

VGAM RNA, also designated SEQ ID:2975.

[15367] Another function of VGAM264 is therefore inhibition of KIAA1323 (Accession XM_032146). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1323. LANO (Accession NM_018214) is another VGAM264 host target gene. LANO BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LANO, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LANO BINDING SITE, designated SEQ ID:20130, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15368] Another function of VGAM264 is therefore inhibition of LANO (Accession NM_018214). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LANO. MGC3101 (Accession NM_024043) is another VGAM264 host target gene. MGC3101 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC3101, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3101 BINDING SITE, designated SEQ ID:23478, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15369] Another function of VGAM264 is therefore inhibition of MGC3101 (Accession NM_024043). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3101. Ring Finger Protein 24 (RNF24, Accession NM_007219) is another VGAM264 host target gene. RNF24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF24 BINDING SITE, designated SEQ ID:14088, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15370] Another function of VGAM264 is therefore inhibition of Ring Finger Protein 24 (RNF24, Accession NM_007219).

Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF24. LOC123346 (Accession XM_063609) is another VGAM264 host target gene. LOC123346 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC123346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC123346 BINDING SITE, designated SEQ ID:37250, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15371] Another function of VGAM264 is therefore inhibition of LOC123346 (Accession XM_063609). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC123346. LOC148932 (Accession XM_086372) is another VGAM264 host target gene. LOC148932 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148932, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC148932 BINDING SITE, designated SEQ ID:38626, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15372] Another function of VGAM264 is therefore inhibition of LOC148932 (Accession XM_086372). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148932. LOC150139 (Accession XM_086794) is another VGAM264 host target gene. LOC150139 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150139 BINDING SITE, designated SEQ ID:38861, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15373] Another function of VGAM264 is therefore inhibition of LOC150139 (Accession XM_086794). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150139. LOC150397 (Accession XM_086907) is an-

other VGAM264 host target gene. LOC150397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150397 BINDING SITE, designated SEQ ID:38961, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15374] Another function of VGAM264 is therefore inhibition of LOC150397 (Accession XM_086907). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150397. LOC152502 (Accession XM_001389) is another VGAM264 host target gene. LOC152502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152502 BINDING SITE, designated SEQ ID:29835, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15375] Another function of VGAM264 is therefore inhibition of LOC152502 (Accession XM_001389). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152502. LOC51667 (Accession NM_016118) is another VGAM264 host target gene. LOC51667 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC51667, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51667 BINDING SITE, designated SEQ ID:18200, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15376] Another function of VGAM264 is therefore inhibition of LOC51667 (Accession NM_016118). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51667. LOC91695 (Accession XM_040084) is another VGAM264 host target gene. LOC91695 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91695, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91695 BINDING SITE, designated SEQ ID:33253, to the nucleotide sequence of VGAM264 RNA, herein designated VGAM RNA, also designated SEQ ID:2975.

[15377] Another function of VGAM264 is therefore inhibition of LOC91695 (Accession XM_040084). Accordingly, utilities of VGAM264 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91695. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 265 (VGAM265) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15378] VGAM265 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM265 was detected is described hereinabove with reference to Figs. 1–8.

[15379] VGAM265 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Callitrichine Herpesvirus 3. VGAM265 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[15380] VGAM265 gene encodes a VGAM265 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM265 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM265 precursor RNA is designated SEQ ID:251, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:251 is located at position 60938 relative to the genome of Calitrichine Herpesvirus 3.

[15381] VGAM265 precursor RNA folds onto itself, forming VGAM265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15382] An enzyme complex designated DICER COMPLEX, `dices` the VGAM265 folded precursor RNA into VGAM265 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM265 RNA is designated SEQ ID:2976, and is provided hereinbelow with reference to the sequence listing part.

[15383] VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM265 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15384] VGAM265 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM265 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM265 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15385] The complementary binding of VGAM265 RNA, herein designated VGAM RNA, to host target binding sites on VGAM265 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM265 host target RNA into VGAM265 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[15386] It is appreciated that VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM265 host target genes. The mRNA of each one of this plurality of VGAM265 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM265 RNA, herein designated VGAM RNA, and which when bound by VGAM265 RNA causes inhibition of translation of respective one or more VGAM265 host target proteins.

[15387] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM265 gene, herein designated VGAM GENE, on one or more VGAM265 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15388] It is yet further appreciated that a function of VGAM265 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of viral infection by Callitrichine Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM265 correlate with, and may be deduced from, the identity of the host target genes which VGAM265 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15389] Nucleotide sequences of the VGAM265 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM265 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM265 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM265 are further described hereinbelow with reference to Table 1.

[15390] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM265 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM265 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15391] As mentioned hereinabove with reference to Fig. 1, a function of VGAM265 gene, herein designated VGAM is inhibition of expression of VGAM265 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM265 correlate with, and may be deduced from, the identity of the target genes which VGAM265 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15392] Epithelial V-like Antigen 1 (EVA1, Accession NM_005797) is a VGAM265 host target gene. EVA1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EVA1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVA1 BINDING SITE, designated SEQ ID:12378, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA,

also designated SEQ ID:2976.

[15393] A function of VGAM265 is therefore inhibition of Epithelial V-like Antigen 1 (EVA1, Accession NM_005797). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVA1. KIAA0630 (Accession XM_114729) is another VGAM265 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43065, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15394] Another function of VGAM265 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. PRO1598 (Accession NM_018503) is another VGAM265 host target gene. PRO1598 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1598, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1598 BINDING SITE, designated SEQ ID:20569, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15395] Another function of VGAM265 is therefore inhibition of PRO1598 (Accession NM_018503). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1598. Squamous Cell Carcinoma Antigen Recognised By T Cells 3 (SART3, Accession NM_014706) is another VGAM265 host target gene. SART3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SART3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SART3 BINDING SITE, designated SEQ ID:16248, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15396] Another function of VGAM265 is therefore inhibition of Squamous Cell Carcinoma Antigen Recognised By T Cells

3 (SART3, Accession NM_014706). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SART3. LOC158450 (Accession XM_088580) is another VGAM265 host target gene. LOC158450 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158450 BINDING SITE, designated SEQ ID:39846, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15397] Another function of VGAM265 is therefore inhibition of LOC158450 (Accession XM_088580). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158450. LOC158504 (Accession XM_088591) is another VGAM265 host target gene. LOC158504 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158504, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC158504 BINDING SITE, designated SEQ ID:39857, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15398] Another function of VGAM265 is therefore inhibition of LOC158504 (Accession XM_088591). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158504. LOC196812 (Accession XM_116868) is another VGAM265 host target gene. LOC196812 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196812, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196812 BINDING SITE, designated SEQ ID:43136, to the nucleotide sequence of VGAM265 RNA, herein designated VGAM RNA, also designated SEQ ID:2976.

[15399] Another function of VGAM265 is therefore inhibition of LOC196812 (Accession XM_116868). Accordingly, utilities of VGAM265 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196812. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 266 (VGAM266) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15400] VGAM266 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM266 was detected is described hereinabove with reference to Figs. 1–8.

[15401] VGAM266 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15402] VGAM266 gene encodes a VGAM266 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM266 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM266 precursor RNA is designated SEQ ID:252, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:252 is

located at position 4402 relative to the genome of Epi-
phyas Postvittana Nucleopolyhedrovirus.

[15403] VGAM266 precursor RNA folds onto itself, forming VGAM266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15404] An enzyme complex designated DICER COMPLEX, `dices` the VGAM266 folded precursor RNA into VGAM266 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM266 RNA is designated SEQ ID:2977, and is provided hereinbelow with reference to the sequence listing part.

[15405] VGAM266 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM266 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15406] VGAM266 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM266 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM266 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM266 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[15407] The complementary binding of VGAM266 RNA, herein designated VGAM RNA, to host target binding sites on VGAM266 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM266 host target RNA into VGAM266 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15408] It is appreciated that VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM266 host target genes. The mRNA of each one of this plurality of VGAM266 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM266 RNA, herein designated VGAM RNA, and which when bound by VGAM266 RNA causes inhibition of translation of respective one or more VGAM266

host target proteins.

[15409] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM266 gene, herein designated VGAM GENE, on one or more VGAM266 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15410] It is yet further appreciated that a function of VGAM266 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucle-

opolyhedrovirus. Specific functions, and accordingly utilities, of VGAM266 correlate with, and may be deduced from, the identity of the host target genes which VGAM266 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15411] Nucleotide sequences of the VGAM266 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM266 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM266 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM266 are further described hereinbelow with reference to Table 1.

[15412] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM266 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM266 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15413] As mentioned hereinabove with reference to Fig. 1, a function of VGAM266 gene, herein designated VGAM is inhibition of expression of VGAM266 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM266 correlate with, and may be deduced from, the identity of the target genes which VGAM266 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15414] Calbindin 1, 28kDa (CALB1, Accession NM_004929) is a VGAM266 host target gene. CALB1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALB1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALB1 BINDING SITE, designated SEQ ID:11367, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15415] A function of VGAM266 is therefore inhibition of Calbindin 1, 28kDa (CALB1, Accession NM_004929), a gene which buffers cytosolic calcium. Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALB1. The function of CALB1 has been established by previous studies. Calbindin is a calcium-binding protein belonging to the troponin C superfamily (see OMIM Ref. No. 191040). It was originally described as a 27-kD protein

induced by vitamin D in the duodenum of the chick. Calbindin immunoreactivity was further detected by radioimmunoassay and immunohistochemistry in the kidney, pancreatic islets, and brain. In the brain, its synthesis is independent of vitamin-D-derived hormones. Two different proteins presenting calbindin immunoreactivity, one of molecular mass 27 kD (now known to be 28 kD) and the other of 29 kD (OMIM Ref. No. 114051), were identified in the central nervous system. Both molecular species are present in the brain of all vertebrates except fish. Parmentier et al. (1987) selected human 28-kD calbindin cDNA clones by antibody screening of lambda-gt11 brain libraries. The sequence showed an open reading frame coding for a protein of 261 amino acids, containing 4 active calcium-binding domains, and 2 modified domains that presumably have lost their calcium-binding capacity. The preliminary data suggested that the 29-kD protein in brain is encoded by a different gene. By means of immunohistochemical methods, Seto-Ohshima et al. (1988) demonstrated a dearth of neurons containing calbindin in the brains of patients with Huntington disease. Calbindin depletion was particularly notable in the neostriatum (caudate nucleus and putamen) of these patients. Parmen-

tier and Vassart (1988) described a HindIII RFLP of the calbindin 28-kilodalton gene. Parmentier et al. (1989) cloned and sequenced the 5-prime and 3-prime regions of the calbindin 28-kD gene and assigned it to chromosome 8 using human-rodent hybrid cell lines. By Southern analysis of somatic cell hybrids and in situ hybridization, Modi et al. (1991) assigned the CALB1 gene to 8p12-q11.2 Parmentier et al. (1991) mapped the CALB1 gene to 8q21.3-q22.1 by in situ hybridization. At the same time, they mapped the CALB2 gene, called by them calretinin, to 16q22-q23, also by in situ hybridization. These localizations matched the chromosomal regions where the carbonic anhydrase isozyme gene cluster (CA1, 114800; CA2, 259730; CA3, 114750) and the related gene CA7 (OMIM Ref. No. 114770) have been mapped, respectively. This suggests that in evolution a common duplication of the calbindin/calretinin and carbonic anhydrase ancestral genes occurred. By computer-assisted analysis of 5 BAC clones and an EST sequence, Tauchi et al. (1999) defined the genomic organization of an 800-kb region on chromosome 8q21 as 5-prime C8ORF1 (OMIM Ref. No. 604598), 3-prime NBS1, 5-prime DECR1 (OMIM Ref. No. 222745), and 3-prime CALB1.

[15416] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15417] Parmentier, M.; Lawson, D. E. M.; Vassart, G. : Human 27-kDa calbindin complementary DNA sequence: evolutionary and functional implications. *Europ. J. Biochem.* 170: 207–215, 1987. ; and

[15418] Seto-Ohshima, A.; Emson, P. C.; Lawson, E.; Mountjoy, C. Q.; Carrasco, L. H. : Loss of matrix calcium-binding protein-containing neurons in Huntington's disease. *Lancet* I: 1252–1254, 198.

[15419] Further studies establishing the function and utilities of CALB1 are found in John Hopkins OMIM database record ID 114050, and in cited publications numbered 1917–192 and 3271 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463) is another VGAM266 host target gene. HNRPDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11947, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15420] Another function of VGAM266 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Interleukin 24 (IL24, Accession NM_006850) is another VGAM266 host target gene. IL24 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL24, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL24 BINDING SITE, designated SEQ ID:13718, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15421] Another function of VGAM266 is therefore inhibition of Interleukin 24 (IL24, Accession NM_006850), a gene which may contribute to terminal cell differentiation. Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL24. The function of IL24 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM258. Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM_000452) is another VGAM266 host target gene. SLC10A2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC10A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC10A2 BINDING SITE, designated SEQ ID:6060, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15422] Another function of VGAM266 is therefore inhibition of Solute Carrier Family 10 (sodium/bile acid cotransporter family), Member 2 (SLC10A2, Accession NM_000452). Ac-

cordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC10A2. Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202) is another VGAM266 host target gene. TCF7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF7 BINDING SITE, designated SEQ ID:9191, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15423] Another function of VGAM266 is therefore inhibition of Transcription Factor 7 (T-cell specific, HMG-box) (TCF7, Accession NM_003202). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF7. DKFZP434P0111 (Accession XM_041116) is another VGAM266 host target gene. DKFZP434P0111 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0111, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0111 BINDING SITE, designated SEQ ID:33452, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15424] Another function of VGAM266 is therefore inhibition of DKFZP434P0111 (Accession XM_041116). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0111. KIAA0495 (Accession XM_031397) is another VGAM266 host target gene. KIAA0495 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0495, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0495 BINDING SITE, designated SEQ ID:31358, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15425] Another function of VGAM266 is therefore inhibition of KIAA0495 (Accession XM_031397). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0495. LOC139221 (Accession XM_066558) is another VGAM266 host target gene. LOC139221 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC139221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139221 BINDING SITE, designated SEQ ID:37330, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15426] Another function of VGAM266 is therefore inhibition of LOC139221 (Accession XM_066558). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139221. LOC257482 (Accession XM_168544) is another VGAM266 host target gene. LOC257482 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC257482, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257482 BINDING SITE, designated SEQ ID:45232, to

the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15427] Another function of VGAM266 is therefore inhibition of LOC257482 (Accession XM_168544). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257482. LOC90346 (Accession NM_138351) is another VGAM266 host target gene. LOC90346 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90346, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90346 BINDING SITE, designated SEQ ID:28746, to the nucleotide sequence of VGAM266 RNA, herein designated VGAM RNA, also designated SEQ ID:2977.

[15428] Another function of VGAM266 is therefore inhibition of LOC90346 (Accession NM_138351). Accordingly, utilities of VGAM266 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90346. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 267 (VGAM267) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15429] VGAM267 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM267 was detected is described hereinabove with reference to Figs. 1–8.

[15430] VGAM267 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15431] VGAM267 gene encodes a VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM267 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM267 precursor RNA is designated SEQ ID:253, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:253 is located at position 87252 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15432] VGAM267 precursor RNA folds onto itself, forming VGAM267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15433] An enzyme complex designated DICER COMPLEX, `dices` the VGAM267 folded precursor RNA into VGAM267 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM267 RNA is designated SEQ ID:2978, and is provided hereinbelow with reference to the sequence listing part.

[15434] VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM267 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM267 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15435] VGAM267 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM267 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM267 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15436] The complementary binding of VGAM267 RNA, herein designated VGAM RNA, to host target binding sites on VGAM267 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM267 host target RNA into VGAM267 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15437] It is appreciated that VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM267 host target genes. The mRNA of each one of this plurality of VGAM267 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM267 RNA, herein designated VGAM RNA, and which when bound by VGAM267 RNA causes inhibition of translation of respective one or more VGAM267 host target proteins.

[15438] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM267 gene, herein designated VGAM GENE, on one or more VGAM267 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15439] It is yet further appreciated that a function of VGAM267 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM267 correlate with, and may be deduced

from, the identity of the host target genes which VGAM267 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15440] Nucleotide sequences of the VGAM267 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM267 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM267 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM267 are further described hereinbelow with reference to Table 1.

[15441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM267 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM267 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15442] As mentioned hereinabove with reference to Fig. 1, a function of VGAM267 gene, herein designated VGAM is inhibition of expression of VGAM267 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM267 correlate with, and may be deduced from, the identity of the target genes which VGAM267

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15443] ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678) is a VGAM267 host target gene. ATP1B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP1B2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP1B2 BINDING SITE, designated SEQ ID:7388, to the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, also designated SEQ ID:2978.

[15444] A function of VGAM267 is therefore inhibition of ATPase, Na⁺/K⁺ Transporting, Beta 2 Polypeptide (ATP1B2, Accession NM_001678), a gene which catalyzes the hydrolysis of ATP coupled with the exchange of Na⁺/K⁺ ions across the plasma membrane. Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP1B2. The function of ATP1B2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM152.KIAA0711 (Accession NM_014867) is another VGAM267 host target gene. KIAA0711 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0711, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0711 BINDING SITE, designated SEQ ID:16957, to the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, also designated SEQ ID:2978.

[15445] Another function of VGAM267 is therefore inhibition of KIAA0711 (Accession NM_014867). Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0711. RDC1 (Accession XM_051522) is another VGAM267 host target gene. RDC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDC1 BINDING SITE, designated SEQ ID:35847, to the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:2978.

[15446] Another function of VGAM267 is therefore inhibition of RDC1 (Accession XM_051522). Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDC1. Vav 3 Oncogene (VAV3, Accession NM_006113) is another VGAM267 host target gene. VAV3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VAV3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VAV3 BINDING SITE, designated SEQ ID:12756, to the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, also designated SEQ ID:2978.

[15447] Another function of VGAM267 is therefore inhibition of Vav 3 Oncogene (VAV3, Accession NM_006113). Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VAV3. LOC147837 (Accession XM_085915) is another VGAM267 host target gene. LOC147837 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147837, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147837 BINDING SITE, designated SEQ ID:38390, to the nucleotide sequence of VGAM267 RNA, herein designated VGAM RNA, also designated SEQ ID:2978.

[15448] Another function of VGAM267 is therefore inhibition of LOC147837 (Accession XM_085915). Accordingly, utilities of VGAM267 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147837. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 268 (VGAM268) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15449] VGAM268 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM268 was detected is described hereinabove with reference to Figs. 1–8.

[15450] VGAM268 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana

Nucleopolyhedrovirus. VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15451] VGAM268 gene encodes a VGAM268 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM268 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM268 precursor RNA is designated SEQ ID:254, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:254 is located at position 84311 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15452] VGAM268 precursor RNA folds onto itself, forming VGAM268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15453] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM268 folded precursor RNA into VGAM268 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 68%) nucleotide sequence of VGAM268 RNA is designated SEQ ID:2979, and is provided hereinbelow with reference to the sequence listing part.

[15454] VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM268 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15455] VGAM268 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM268 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM268 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15456] The complementary binding of VGAM268 RNA, herein designated VGAM RNA, to host target binding sites on VGAM268 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM268 host target RNA into VGAM268 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15457] It is appreciated that VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM268 host target genes. The mRNA of each one of this plurality of VGAM268 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM268 RNA, herein designated VGAM RNA, and which when bound by VGAM268 RNA causes inhibition of translation of respective one or more VGAM268 host target proteins.

[15458] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM268 gene, herein designated VGAM GENE, on one or more VGAM268 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15459] It is yet further appreciated that a function of VGAM268 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM268 correlate with, and may be deduced from, the identity of the host target genes which VGAM268 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15460] Nucleotide sequences of the VGAM268 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM268 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM268 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM268 are further described hereinbelow with reference to Table 1.

[15461] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM268 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM268 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15462] As mentioned hereinabove with reference to Fig. 1, a function of VGAM268 gene, herein designated VGAM is inhibition of expression of VGAM268 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM268 correlate with, and may be deduced from, the identity of the target genes which VGAM268 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15463] Neuronal Cell Adhesion Molecule (NRCAM, Accession NM_005010) is a VGAM268 host target gene. NRCAM BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NRCAM, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRCAM BINDING SITE, designated SEQ ID:11449, to the

nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15464] A function of VGAM268 is therefore inhibition of Neuronal Cell Adhesion Molecule (NRCAM, Accession NM_005010), a gene which functions as a cell surface protein and belongs to the immunoglobulin superfamily. Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRCAM. The function of NRCAM has been established by previous studies. The cell adhesion molecules (CAMs) are a subset of the immunoglobulin (Ig) superfamily found in the nervous systems of both vertebrates and invertebrates. They are usually surface membrane proteins with multiple Ig domains at their N termini followed by several fibronectin type III repeats and either a transmembrane intracellular domain or a glycoposphatidylinositol-linked membrane anchor at the C terminus (Lane et al., 1996). The chicken Bravo/Nr-CAM was described by Grumet et al. (1991) and Kayyem et al. (1992) and shown to play a role in nervous system development. The protein interacts with other cell surface molecules of the Ig superfamily and appears to be necessary for specific pathfinding by axonal growth cones during development (Lane et al., 1996).

Lane et al. (1996) cloned the human homolog (NRCAM) of the chicken gene from a fetal brain library. Like its chicken counterpart, the predicted 1,275–amino acid protein has 6 V–like Ig domains and 5 fibronectin type III repeats. The transmembrane and intracellular domains of human and chicken NRCAM are entirely conserved and the proteins are 82% identical overall. Alternative splice variants were observed involving sequence around the fifth fibronectin repeat. Northern blots showed an approximately 7–kb transcript in all tissues of adult human brain examined.

[15465] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15466] Kayyem, J. F.; Roman, J. M.; de la Rosa, E. J.; Schwarz, U.; Dreyer, W. J. : Bravo/Nr–CAM is closely related to the cell adhesion molecules L1 and Ng–CAM and has a similar heterodimer structure. *J. Cell. Biol.* 118: 1259–1270, 1992. ; and

[15467] Lane, R. P.; Chen, X.–N.; Yamakawa, K.; Vielmetter, J.; Korenberg, J. R.; Dreyer, W. J. : Characterization of a highly conserved human homolog to the chicken neural cell surface protein.

[15468] Further studies establishing the function and utilities of

NRCAM are found in John Hopkins OMIM database record ID 601581, and in cited publications numbered 6535–6539 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP586P0123 (Accession XM_170681) is another VGAM268 host target gene. DKFZP586P0123 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP586P0123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP586P0123 BINDING SITE, designated SEQ ID:45466, to the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15469] Another function of VGAM268 is therefore inhibition of DKFZP586P0123 (Accession XM_170681). Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP586P0123. MP1 (Accession NM_014968) is another VGAM268 host target gene. MP1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MP1, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MP1 BINDING SITE, designated SEQ ID:17359, to the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15470] Another function of VGAM268 is therefore inhibition of MP1 (Accession NM_014968). Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MP1. Phorbol-12-myristate-13-acetate-induced Protein 1 (PMAIP1, Accession NM_021127) is another VGAM268 host target gene. PMAIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PMAIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PMAIP1 BINDING SITE, designated SEQ ID:22100, to the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15471] Another function of VGAM268 is therefore inhibition of Phorbol-12-myristate-13-acetate-induced Protein 1

(PMAIP1, Accession NM_021127). Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PMAIP1. Rpo1-2 (Accession NM_019014) is another VGAM268 host target gene. Rpo1-2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rpo1-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rpo1-2 BINDING SITE, designated SEQ ID:21098, to the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15472] Another function of VGAM268 is therefore inhibition of Rpo1-2 (Accession NM_019014). Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with Rpo1-2. LOC220002 (Accession XM_166224) is another VGAM268 host target gene. LOC220002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of LOC220002 BINDING SITE, designated SEQ ID:44048, to the nucleotide sequence of VGAM268 RNA, herein designated VGAM RNA, also designated SEQ ID:2979.

[15473] Another function of VGAM268 is therefore inhibition of LOC220002 (Accession XM_166224). Accordingly, utilities of VGAM268 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220002. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 269 (VGAM269) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15474] VGAM269 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM269 was detected is described hereinabove with reference to Figs. 1–8.

[15475] VGAM269 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene

contained in the human genome.

[15476] VGAM269 gene encodes a VGAM269 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM269 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM269 precursor RNA is designated SEQ ID:255, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:255 is located at position 10259 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15477] VGAM269 precursor RNA folds onto itself, forming VGAM269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15478] An enzyme complex designated DICER COMPLEX, `dices` the VGAM269 folded precursor RNA into VGAM269 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM269 RNA is designated SEQ ID:2980, and is provided hereinbelow with reference to the sequence listing part.

[15479] VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM269 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15480] VGAM269 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM269 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM269 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15481] The complementary binding of VGAM269 RNA, herein designated VGAM RNA, to host target binding sites on VGAM269 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM269 host target RNA into VGAM269 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15482] It is appreciated that VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM269 host target genes. The mRNA of each one of this plurality of VGAM269 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM269 RNA, herein designated VGAM RNA, and which when bound by VGAM269 RNA causes inhibition of translation of respective one or more VGAM269 host target proteins.

[15483] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM269 gene, herein designated VGAM GENE, on one or more VGAM269 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15484] It is yet further appreciated that a function of VGAM269 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM269 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM269 correlate with, and may be deduced from, the identity of the host target genes which VGAM269 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15485] Nucleotide sequences of the VGAM269 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM269 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM269 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM269 are further described hereinbelow with reference to Table 1.

[15486] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM269 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM269 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15487] As mentioned hereinabove with reference to Fig. 1, a function of VGAM269 gene, herein designated VGAM is inhibition of expression of VGAM269 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM269 correlate with, and may be deduced from, the identity of the target genes which VGAM269 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15488] Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM_016255) is a VGAM269 host target gene. FAM8A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FAM8A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FAM8A1 BINDING SITE, designated SEQ ID:18380, to the nucleotide sequence of VGAM269 RNA, herein designated VGAM RNA, also designated SEQ

ID:2980.

[15489] A function of VGAM269 is therefore inhibition of Family with Sequence Similarity 8, Member A1 (FAM8A1, Accession NM_016255). Accordingly, utilities of VGAM269 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FAM8A1. IMP-2 (Accession NM_006548) is another VGAM269 host target gene. IMP-2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IMP-2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IMP-2 BINDING SITE, designated SEQ ID:13305, to the nucleotide sequence of VGAM269 RNA, herein designated VGAM RNA, also designated SEQ ID:2980.

[15490] Another function of VGAM269 is therefore inhibition of IMP-2 (Accession NM_006548). Accordingly, utilities of VGAM269 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IMP-2. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger

270 (VGAM270) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15491] VGAM270 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM270 was detected is described hereinabove with reference to Figs. 1–8.

[15492] VGAM270 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15493] VGAM270 gene encodes a VGAM270 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM270 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM270 precursor RNA is designated SEQ ID:256, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:256 is located at position 21071 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15494] VGAM270 precursor RNA folds onto itself, forming

VGAM270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15495] An enzyme complex designated DICER COMPLEX, `dices` the VGAM270 folded precursor RNA into VGAM270 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM270 RNA is designated SEQ ID:2981, and is provided hereinbelow with reference to the sequence listing part.

[15496] VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM270 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15497] VGAM270 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM270 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM270 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15498] The complementary binding of VGAM270 RNA, herein designated VGAM RNA, to host target binding sites on VGAM270 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM270 host target RNA into VGAM270 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15499] It is appreciated that VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM270 host target genes. The mRNA of each one of this plurality of VGAM270 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM270 RNA, herein designated VGAM RNA, and which when bound by VGAM270 RNA causes inhibition of translation of respective one or more VGAM270 host target proteins.

[15500] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM270 gene, herein designated VGAM GENE, on one or more VGAM270 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15501] It is yet further appreciated that a function of VGAM270 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM270 correlate with, and may be deduced from, the identity of the host target genes which

VGAM270 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15502] Nucleotide sequences of the VGAM270 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM270 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM270 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM270 are further described hereinbelow with reference to Table 1.

[15503] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM270 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM270 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15504] As mentioned hereinabove with reference to Fig. 1, a function of VGAM270 gene, herein designated VGAM is inhibition of expression of VGAM270 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM270 correlate with, and may be deduced from, the identity of the target genes which VGAM270 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[15505] FREB (Accession NM_032738) is a VGAM270 host target gene. FREB BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FREB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FREB BINDING SITE, designated SEQ ID:26467, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15506] A function of VGAM270 is therefore inhibition of FREB (Accession NM_032738). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FREB. FLJ12610 (Accession NM_024782) is another VGAM270 host target gene. FLJ12610 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ12610, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12610 BINDING SITE, designated SEQ ID:24151, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also design-

nated SEQ ID:2981.

[15507] Another function of VGAM270 is therefore inhibition of FLJ12610 (Accession NM_024782). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12610. RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733) is another VGAM270 host target gene. RAB40A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB40A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40A BINDING SITE, designated SEQ ID:39932, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15508] Another function of VGAM270 is therefore inhibition of RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40A. LOC131870 (Accession XM_059544) is another VGAM270 host target gene. LOC131870 BINDING SITE is HOST TARGET binding

site found in the 3' untranslated region of mRNA encoded by LOC131870, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC131870 BINDING SITE, designated SEQ ID:37018, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15509] Another function of VGAM270 is therefore inhibition of LOC131870 (Accession XM_059544). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC131870. LOC154222 (Accession XM_098497) is another VGAM270 host target gene. LOC154222 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154222 BINDING SITE, designated SEQ ID:41693, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15510] Another function of VGAM270 is therefore inhibition of

LOC154222 (Accession XM_098497). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154222. LOC155064 (Accession XM_088128) is another VGAM270 host target gene. LOC155064 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155064, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155064 BINDING SITE, designated SEQ ID:39529, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15511] Another function of VGAM270 is therefore inhibition of LOC155064 (Accession XM_088128). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155064. LOC201194 (Accession XM_117061) is another VGAM270 host target gene. LOC201194 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201194, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC201194 BINDING SITE, designated SEQ ID:43218, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15512] Another function of VGAM270 is therefore inhibition of LOC201194 (Accession XM_117061). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201194. LOC91351 (Accession XM_037817) is another VGAM270 host target gene. LOC91351 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC91351, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91351 BINDING SITE, designated SEQ ID:32700, to the nucleotide sequence of VGAM270 RNA, herein designated VGAM RNA, also designated SEQ ID:2981.

[15513] Another function of VGAM270 is therefore inhibition of LOC91351 (Accession XM_037817). Accordingly, utilities of VGAM270 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91351. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 271 (VGAM271) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15514] VGAM271 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM271 was detected is described hereinabove with reference to Figs. 1–8.

[15515] VGAM271 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15516] VGAM271 gene encodes a VGAM271 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM271 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM271 precursor RNA is designated SEQ ID:257, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:257 is

located at position 113843 relative to the genome of Epi-
phyas Postvittana Nucleopolyhedrovirus.

[15517] VGAM271 precursor RNA folds onto itself, forming VGAM271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15518] An enzyme complex designated DICER COMPLEX, `dices` the VGAM271 folded precursor RNA into VGAM271 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM271 RNA is designated SEQ ID:2982, and is provided hereinbelow with reference to the sequence listing part.

[15519] VGAM271 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM271 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15520] VGAM271 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM271 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM271 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM271 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15521] The complementary binding of VGAM271 RNA, herein designated VGAM RNA, to host target binding sites on VGAM271 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM271 host target RNA into VGAM271 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15522] It is appreciated that VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM271 host target genes. The mRNA of each one of this plurality of VGAM271 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM271 RNA, herein designated VGAM RNA, and which when bound by VGAM271 RNA causes inhibition of translation of respective one or more VGAM271

host target proteins.

[15523] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM271 gene, herein designated VGAM GENE, on one or more VGAM271 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15524] It is yet further appreciated that a function of VGAM271 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucle-

opolyhedrovirus. Specific functions, and accordingly utilities, of VGAM271 correlate with, and may be deduced from, the identity of the host target genes which VGAM271 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15525] Nucleotide sequences of the VGAM271 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM271 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM271 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM271 are further described hereinbelow with reference to Table 1.

[15526] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM271 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM271 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15527] As mentioned hereinabove with reference to Fig. 1, a function of VGAM271 gene, herein designated VGAM is inhibition of expression of VGAM271 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM271 correlate with, and may be deduced from, the identity of the target genes which VGAM271 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15528] Solute Carrier Family 25 (mitochondrial carrier, Aralar), Member 12 (SLC25A12, Accession NM_003705) is a VGAM271 host target gene. SLC25A12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC25A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC25A12 BINDING SITE, designated SEQ ID:9805, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15529] A function of VGAM271 is therefore inhibition of Solute Carrier Family 25 (mitochondrial carrier, Aralar), Member 12 (SLC25A12, Accession NM_003705), a gene which is a calcium -dependent mitochondrial solute carrier. may have a function in the urea cycle (by similarity). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC25A12. The function of SLC25A12 has been es-

established by previous studies. The mitochondrial inner membrane harbors a set of carrier proteins for metabolite transport that constitute a superfamily of related proteins. The yeast open reading frame YNL083W encodes a predicted protein with characteristics of both mitochondrial carrier and calcium-binding proteins. By searching EST databases for proteins with similar features, del Arco and Satrustegui (1998) identified several *C. elegans* cDNAs encoding putative calcium-dependent mitochondrial carrier proteins. Using the sequence of one of the *C. elegans* cDNAs, the authors searched human EST databases and found cDNAs encoding a related human protein that they designated 'Aralar' (formed by combining the given name of the first author, 'Araceli,' with a Spanish word meaning 'very long,' 'hiperlarga'). The N-terminal portion of the predicted 678-amino acid Aralar protein contains 3 canonical EF-hand calcium-binding domains and 2 imperfect EF-hand domains. The authors demonstrated that this half of the protein bound calcium in vitro. The C-terminal half of Aralar shares 28 to 29% identity with proteins of the mitochondrial solute carrier family, including oxoglutarate/malate carrier (OMIM Ref. No. 604165), ADP/ATP translocase-2 (OMIM Ref. No. 300150), UCP1

(OMIM Ref. No. 113730), and tricarboxylate carrier (OMIM Ref. No. 190315). Like the other mitochondrial carrier proteins, the C-terminal region of Aralar contains 6 potential transmembrane domains. Immunocytochemistry and cell fractionation studies showed that both exogenously expressed and endogenous Aralar protein are localized within the mitochondria. Northern blot analysis revealed that Aralar is expressed as 2.9- and 3.2-kb mRNAs predominantly in heart and skeletal muscle, with weaker expression in brain and kidney. Del Arco and Satrustegui (1998) concluded that the domain structure, mitochondrial localization, and expression in excitable tissues of Aralar suggest a possible function for this protein as a calcium-dependent mitochondrial solute carrier. Crackower et al. (1999) mapped the SLC25A12 gene to chromosome 2q24 by FISH, somatic cell and radiation hybrid mapping, and YAC clone analyses. Sanz et al. (2000) localized the SLC25A12 gene to 2q31 by FISH.

[15530] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15531] del Arco, A.; Satrustegui, J. : Molecular cloning of aralar, a new member of the mitochondrial carrier superfamily that

binds calcium and is present in human muscle and brain.

J. Biol. Chem. 273: 23327–23334, 1998. ; and

[15532] Crackower, M. A.; Sinasac, D. S.; Lee, J. R.; Herbrick, J.–A.; Tsui, L.–C.; Scherer, S. W. : Assignment of the SLC25A12 gene coding for the human calcium–binding mitochondrial solute carrier.

[15533] Further studies establishing the function and utilities of SLC25A12 are found in John Hopkins OMIM database record ID 603667, and in cited publications numbered 989–991 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM271 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31078, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15534] Another function of VGAM271 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577).

Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. F-box Only Protein 21 (FBXO21, Accession NM_033624) is another VGAM271 host target gene. FBXO21 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FBXO21, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO21 BINDING SITE, designated SEQ ID:27321, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15535] Another function of VGAM271 is therefore inhibition of F-box Only Protein 21 (FBXO21, Accession NM_033624). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO21. FLJ22601 (Accession NM_024822) is another VGAM271 host target gene. FLJ22601 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22601, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of FLJ22601 BINDING SITE, designated SEQ ID:24211, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15536] Another function of VGAM271 is therefore inhibition of FLJ22601 (Accession NM_024822). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22601. Interleukin 10 Receptor, Beta (IL10RB, Accession NM_000628) is another VGAM271 host target gene. IL10RB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL10RB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL10RB BINDING SITE, designated SEQ ID:6244, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15537] Another function of VGAM271 is therefore inhibition of Interleukin 10 Receptor, Beta (IL10RB, Accession NM_000628). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clini-

cal conditions associated with IL10RB. MGC13102 (Accession NM_032323) is another VGAM271 host target gene. MGC13102 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC13102, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13102 BINDING SITE, designated SEQ ID:26134, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15538] Another function of VGAM271 is therefore inhibition of MGC13102 (Accession NM_032323). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13102. SPEC1 (Accession NM_020239) is another VGAM271 host target gene. SPEC1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SPEC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPEC1 BINDING SITE, designated SEQ ID:21509, to the nucleotide sequence of

VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15539] Another function of VGAM271 is therefore inhibition of SPEC1 (Accession NM_020239). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPEC1. LOC147645 (Accession XM_085831) is another VGAM271 host target gene. LOC147645 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147645, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147645 BINDING SITE, designated SEQ ID:38357, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15540] Another function of VGAM271 is therefore inhibition of LOC147645 (Accession XM_085831). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147645. LOC150378 (Accession XM_086857) is another VGAM271 host target gene. LOC150378 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC150378, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150378 BINDING SITE, designated SEQ ID:38921, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15541] Another function of VGAM271 is therefore inhibition of LOC150378 (Accession XM_086857). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150378. LOC152313 (Accession XM_098190) is another VGAM271 host target gene. LOC152313 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152313, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152313 BINDING SITE, designated SEQ ID:41474, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15542] Another function of VGAM271 is therefore inhibition of LOC152313 (Accession XM_098190). Accordingly, utilities

of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152313. LOC164397 (Accession XM_092780) is another VGAM271 host target gene. LOC164397 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC164397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164397 BINDING SITE, designated SEQ ID:40150, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15543] Another function of VGAM271 is therefore inhibition of LOC164397 (Accession XM_092780). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164397. LOC220763 (Accession XM_055551) is another VGAM271 host target gene. LOC220763 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC220763, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC220763 BINDING SITE, designated SEQ ID:36301, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15544] Another function of VGAM271 is therefore inhibition of LOC220763 (Accession XM_055551). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220763. LOC90317 (Accession XM_030892) is another VGAM271 host target gene. LOC90317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90317 BINDING SITE, designated SEQ ID:31206, to the nucleotide sequence of VGAM271 RNA, herein designated VGAM RNA, also designated SEQ ID:2982.

[15545] Another function of VGAM271 is therefore inhibition of LOC90317 (Accession XM_030892). Accordingly, utilities of VGAM271 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90317. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 272 (VGAM272) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15546] VGAM272 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM272 was detected is described hereinabove with reference to Figs. 1–8.

[15547] VGAM272 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15548] VGAM272 gene encodes a VGAM272 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM272 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM272 precursor RNA is designated SEQ ID:258, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:258 is located at position 105105 relative to the genome of Epi-

phyas Postvittana Nucleopolyhedrovirus.

[15549] VGAM272 precursor RNA folds onto itself, forming VGAM272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15550] An enzyme complex designated DICER COMPLEX, `dices` the VGAM272 folded precursor RNA into VGAM272 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM272 RNA is designated SEQ ID:2983, and is provided hereinbelow with reference to the sequence listing part.

[15551] VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM272 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15552] VGAM272 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM272 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM272 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15553] The complementary binding of VGAM272 RNA, herein designated VGAM RNA, to host target binding sites on VGAM272 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM272 host target RNA into VGAM272 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15554] It is appreciated that VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM272 host target genes. The mRNA of each one of this plurality of VGAM272 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM272 RNA, herein designated VGAM RNA, and which when bound by VGAM272 RNA causes inhibition of translation of respective one or more VGAM272 host target proteins.

[15555] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM272 gene, herein designated VGAM GENE, on one or more VGAM272 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15556] It is yet further appreciated that a function of VGAM272 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utili-

ties, of VGAM272 correlate with, and may be deduced from, the identity of the host target genes which VGAM272 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15557] Nucleotide sequences of the VGAM272 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM272 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM272 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM272 are further described hereinbelow with reference to Table 1.

[15558] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM272 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM272 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15559] As mentioned hereinabove with reference to Fig. 1, a function of VGAM272 gene, herein designated VGAM is inhibition of expression of VGAM272 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM272 correlate with, and may be deduced

from, the identity of the target genes which VGAM272 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15560] Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450) is a VGAM272 host target gene. KLHL3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL3 BINDING SITE, designated SEQ ID:42270, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15561] A function of VGAM272 is therefore inhibition of Kelch-like 3 (Drosophila) (KLHL3, Accession XM_113450). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL3. Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727) is another VGAM272 host target gene. SLC24A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC24A1, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC24A1 BINDING SITE, designated SEQ ID:11100, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15562] Another function of VGAM272 is therefore inhibition of Solute Carrier Family 24 (sodium/potassium/calcium exchanger), Member 1 (SLC24A1, Accession NM_004727), a gene which is a critical component of the visual transduction cascade, controlling the calcium concentration of outer segments during light and darkness. Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC24A1. The function of SLC24A1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM142. Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169) is another VGAM272 host target gene. SUFU BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SUFU, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SUFU BINDING SITE, designated SEQ ID:18255, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15563] Another function of VGAM272 is therefore inhibition of Suppressor of Fused Homolog (Drosophila) (SUFU, Accession NM_016169). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SUFU. ADP-ribosylation Factor GTPase Activating Protein 1 (ARFGAP1, Accession NM_018209) is another VGAM272 host target gene. ARFGAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARFGAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARFGAP1 BINDING SITE, designated SEQ ID:20110, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15564] Another function of VGAM272 is therefore inhibition of ADP-ribosylation Factor GTPase Activating Protein 1

(ARFGAP1, Accession NM_018209). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARFGAP1. Cyclin E2 (CCNE2, Accession NM_057749) is another VGAM272 host target gene. CCNE2 BINDING SITE1 and CCNE2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CCNE2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCNE2 BINDING SITE1 and CCNE2 BINDING SITE2, designated SEQ ID:27711 and SEQ ID:11050 respectively, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15565] Another function of VGAM272 is therefore inhibition of Cyclin E2 (CCNE2, Accession NM_057749). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCNE2. KIAA0553 (Accession XM_045981) is another VGAM272 host target gene. KIAA0553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0553, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0553 BINDING SITE, designated SEQ ID:34638, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15566] Another function of VGAM272 is therefore inhibition of KIAA0553 (Accession XM_045981). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0553. KIAA1200 (Accession XM_031054) is another VGAM272 host target gene. KIAA1200 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1200, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1200 BINDING SITE, designated SEQ ID:31264, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15567] Another function of VGAM272 is therefore inhibition of KIAA1200 (Accession XM_031054). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1200. MGC12760 (Accession NM_032723) is another VGAM272 host target gene. MGC12760 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by MGC12760, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12760 BINDING SITE, designated SEQ ID:26450, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15568] Another function of VGAM272 is therefore inhibition of MGC12760 (Accession NM_032723). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12760. LOC153505 (Accession XM_087693) is another VGAM272 host target gene. LOC153505 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC153505, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153505 BINDING SITE, designated SEQ ID:39383, to

the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15569] Another function of VGAM272 is therefore inhibition of LOC153505 (Accession XM_087693). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153505. LOC157503 (Accession XM_098767) is another VGAM272 host target gene. LOC157503 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC157503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC157503 BINDING SITE, designated SEQ ID:41812, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15570] Another function of VGAM272 is therefore inhibition of LOC157503 (Accession XM_098767). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC157503. LOC162333 (Accession XM_102591) is another VGAM272 host target gene. LOC162333 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42128, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15571] Another function of VGAM272 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC253782 (Accession XM_171023) is another VGAM272 host target gene. LOC253782 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253782, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253782 BINDING SITE, designated SEQ ID:45797, to the nucleotide sequence of VGAM272 RNA, herein designated VGAM RNA, also designated SEQ ID:2983.

[15572] Another function of VGAM272 is therefore inhibition of LOC253782 (Accession XM_171023). Accordingly, utilities

of VGAM272 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253782. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 273 (VGAM273) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15573] VGAM273 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM273 was detected is described hereinabove with reference to Figs. 1–8.

[15574] VGAM273 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15575] VGAM273 gene encodes a VGAM273 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM273 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM273 precursor RNA is designated SEQ ID:259, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:259 is located at position 90664 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15576] VGAM273 precursor RNA folds onto itself, forming VGAM273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15577] An enzyme complex designated DICER COMPLEX, `dices` the VGAM273 folded precursor RNA into VGAM273 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM273 RNA is designated SEQ ID:2984, and

is provided hereinbelow with reference to the sequence listing part.

[15578] VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM273 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15579] VGAM273 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM273 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM273 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15580] The complementary binding of VGAM273 RNA, herein designated VGAM RNA, to host target binding sites on VGAM273 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM273 host target RNA into VGAM273 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15581] It is appreciated that VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM273 host target genes. The mRNA of each one of this plurality of VGAM273 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM273 RNA, herein designated VGAM RNA, and which when bound by VGAM273 RNA causes inhibition of translation of respective one or more VGAM273 host target proteins.

[15582] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM273 gene, herein designated VGAM GENE, on one or more VGAM273 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15583] It is yet further appreciated that a function of VGAM273 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM273 correlate with, and may be deduced from, the identity of the host target genes which VGAM273 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15584] Nucleotide sequences of the VGAM273 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM273 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM273 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM273 are further described hereinbelow with reference to Table 1.

[15585] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM273 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM273 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15586] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM273 gene, herein designated VGAM is inhibition of expression of VGAM273 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM273 correlate with, and may be deduced from, the identity of the target genes which VGAM273 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15587] Fibroblast Growth Factor 23 (FGF23, Accession NM_020638) is a VGAM273 host target gene. FGF23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FGF23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FGF23 BINDING SITE, designated SEQ ID:21794, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15588] A function of VGAM273 is therefore inhibition of Fibroblast Growth Factor 23 (FGF23, Accession NM_020638), a gene which is a member of the fibroblast growth factor family. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF23. The function of FGF23 and

its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM24. Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM_018658) is another VGAM273 host target gene. KCNJ16 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNJ16, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNJ16 BINDING SITE, designated SEQ ID:20729, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15589] Another function of VGAM273 is therefore inhibition of Potassium Inwardly-rectifying Channel, Subfamily J, Member 16 (KCNJ16, Accession NM_018658). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNJ16. Lactate Dehydrogenase B (LDHB, Accession NM_002300) is another VGAM273 host target gene. LDHB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LDHB, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LDHB BINDING SITE, designated SEQ ID:8087, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15590] Another function of VGAM273 is therefore inhibition of Lactate Dehydrogenase B (LDHB, Accession NM_002300), a gene which causes dehydrogenation of lactate. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LDHB. The function of LDHB has been established by previous studies. LDHB and peptidase B (OMIM Ref. No. 169900) are linked (Santachiara et al., 1970) and both loci are on chromosome 12 (Chen et al., 1973). Kitamura et al. (1971) reported the first case of a complete deficiency of lactate dehydrogenase subunit H(B) in serum, saliva and erythrocytes of a 64-year-old male with mild diabetes. Study made on family members revealed low LDH activity in their serum also linked with decreased relative activity of the H4(B4) fraction. Based on the comparison of the calculated ratio of H to M subunits in normal and affected family members, it was hypothesized

that the proband is homozygous while the abnormal family members are heterozygous, assuming a single gene is involved. Red cell metabolism in the proband was studied by Miwa et al. (1971); neither reticulocytosis nor hemolytic anemia was present. Thus, although LDHA deficiency leads to myoglobinuria and risk of renal failure after strenuous exercise, LDHB deficiency probably has no clear symptomatic consequences. As pointed out by Sudo (1993), LDH deficiency is of interest to laboratory medicine mainly because it can cause misdiagnosis in those disorders in which elevation of serum LDH is expected. LDH deficiency can probably be considered a 'nondisease.' In a screening of 2,880 blood samples from healthy persons in the Fukuoka Prefecture in Japan, Maekawa et al. (1994) found that the frequency of heterozygotes for either LDHA or LDHB deficiency was 0.104% at each locus. These estimated frequencies were slightly lower than, but not significantly different from, those found previously in the Shizuoka Prefecture. In a case of deletion of the short arm of chromosome 12, Weiss et al. (1973) found evidence that LDHB is located there. From study of somatic cell hybrids Hamerton et al. (1975) concluded that LDHB is in the 12q21-pter region.

Rethore et al. (1975) found augmentation of LDHB activity in a boy trisomic for the short arm of chromosome 12. From study of 3 patients with different deletions of chromosome 12, Rethore et al. (1976) concluded that the G3PD locus is on the distal part of 12p, between p12.2 and 12pter, and that the LDHB locus is on the middle third between 12p12.1 and 12p12.2. The results for TPI were similar to those for G3PD, suggesting the same distal localization. Mohrenweiser and Neel (1981) identified thermolabile variants of lactate dehydrogenase B, glucosephosphate isomerase, and glucose-6-phosphate dehydrogenase. None was detectable as a variant by standard electrophoretic techniques. All were inherited. Steinbach and Rehder (1987) demonstrated dosage effect with LDHB in a case of tetrasomy of 12p. Sakai et al. (1987) isolated and sequenced LDHB cDNA. Nucleotide and amino acid sequences showed 68% and 75% identity, respectively, with those of LDHA. Sudo et al. (1990) demonstrated 93% homology between an LDHB processed pseudogene and the functional gene. The pseudogene was mapped to the X chromosome by dot blot analysis.

[15591] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [15592] Kitamura, M.; Iijima, N.; Hashimoto, F.; Hiratsuka, A. : Hereditary deficiency of subunit H of lactate dehydrogenase. Clin. Chim. Acta 34: 419–423, 1971. ; and
- [15593] Sudo, K.; Maekawa, M.; Luedemann, M. M.; Deaven, L. L.; Li, S. S.–L. : Human lactate dehydrogenase–B processed pseudogene: nucleotide sequence analysis and assignment to the X–chromosom.
- [15594] Further studies establishing the function and utilities of LDHB are found in John Hopkins OMIM database record ID 150100, and in cited publications numbered 5076, 11205–11214, 1127 and 11290–11301 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Opioid Binding Protein/cell Adhesion Molecule–like (OPCML, Accession NM_002545) is another VGAM273 host target gene. OPCML BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by OPCML, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPCML BINDING SITE, designated SEQ ID:8396, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also desig–

nated SEQ ID:2984.

[15595] Another function of VGAM273 is therefore inhibition of Opioid Binding Protein/cell Adhesion Molecule-like (OPCML, Accession NM_002545), a gene which may function as a GPI-anchored neural cell adhesion molecule. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPCML. The function of OPCML and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM71. Protein Kinase, CAMP-dependent, Catalytic, Alpha (PRKACA, Accession NM_002730) is another VGAM273 host target gene. PRKACA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRKACA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKACA BINDING SITE, designated SEQ ID:8597, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15596] Another function of VGAM273 is therefore inhibition of

Protein Kinase, CAMP-dependent, Catalytic, Alpha (PRKACA, Accession NM_002730), a gene which phosphorylates target proteins on serine or threonine residues. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKACA. The function of PRKACA and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM175. Rho-associated, Coiled-coil Containing Protein Kinase 2 (ROCK2, Accession XM_038377) is another VGAM273 host target gene. ROCK2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ROCK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ROCK2 BINDING SITE, designated SEQ ID:32835, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15597] Another function of VGAM273 is therefore inhibition of Rho-associated, Coiled-coil Containing Protein Kinase 2 (ROCK2, Accession XM_038377), a gene which regulates

cytokinesis, smooth muscle contraction, the formation of actin stress fibers and focal adhesions. Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ROCK2. The function of ROCK2 has been established by previous studies. ROCK2 is a serine/threonine kinase that regulates cytokinesis, smooth muscle contraction, the formation of actin stress fibers and focal adhesions, and the activation of the c-fos (OMIM Ref. No. 164810) serum response element. ROCK2, which is an isozyme of ROCK1 (OMIM Ref. No. 601702), is a target for the small GTPase Rho (e.g., 165390). Nakamura et al. (2001) studied the role of Rho in the migration of corneal epithelial cells in rabbit. They detected both ROCK1 (OMIM Ref. No. 601702) and ROCK2 in the corneal epithelium at protein and mRNA levels. They found that exoenzyme C3, a Rho inhibitor, inhibits corneal epithelial migration in a dose-dependent manner and prevents the stimulatory effect of the Rho activator lysophosphatidic acid (LPA). Both cytochalasin B, an inhibitor of actin filament assembly, and ML7, an inhibitor of myosin light chain kinase, also prevent LPA stimulation of epithelial migration. The authors suggested that Rho mediates corneal epithelial migration

in response to external stimuli by regulating the organization of the actin cytoskeleton. Rao et al. (2001) investigated the role of Rho kinase in the modulation of aqueous humor outflow facility. The treatment of human trabecular meshwork and canal of Schlemm cells with a Rho kinase-specific inhibitor led to significant but reversible changes in cell shape and decreased actin stress fibers, focal adhesions, and protein phosphotyrosine staining. Based on the Rho kinase inhibitor-induced changes in myosin light chain phosphorylation and actomyosin organization, the authors suggested that cellular relaxation and loss of cell-substratum adhesions in the human trabecular meshwork and canal of Schlemm cells could result in either increased paracellular fluid flow across the canal of Schlemm or altered flow pathway through the juxtacanalicular tissue, thereby lowering resistance to outflow. They suggested Rho kinase as a potential target for the development of drugs to modulate intraocular pressure in glaucoma patients.

[15598] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15599] Nakamura, M.; Nagano, T.; Chikama, T.; Nishida, T. : Role

of the small GTP-binding protein Rho in epithelial cell migration in the rabbit cornea. Invest. Ophthalm. Vis. Sci. 42: 941-947, 2001. ; and

[15600] Rao, P. V.; Deng, P.-F.; Kumar, J.; Epstein, D. L. : Modulation of aqueous humor outflow facility by the Rho kinase-specific inhibitor Y-27632. Invest. Ophthalm. Vis. Sci. 42: 1029-1037.

[15601] Further studies establishing the function and utilities of ROCK2 are found in John Hopkins OMIM database record ID 604002, and in cited publications numbered 9440, 10912-1091 and 7392 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cysteine and Tyrosine-rich 1 (CYR1, Accession NM_052954) is another VGAM273 host target gene. CYR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYR1 BINDING SITE, designated SEQ ID:27514, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15602] Another function of VGAM273 is therefore inhibition of Cysteine and Tyrosine-rich 1 (CYR1, Accession NM_052954). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYR1. KIAA1036 (Accession NM_014909) is another VGAM273 host target gene. KIAA1036 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1036, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1036 BINDING SITE, designated SEQ ID:17126, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15603] Another function of VGAM273 is therefore inhibition of KIAA1036 (Accession NM_014909). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1036. SBBI31 (Accession NM_014035) is another VGAM273 host target gene. SBBI31 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SBBI31, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SBBI31 BINDING SITE, designated SEQ ID:15266, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15604] Another function of VGAM273 is therefore inhibition of SBBI31 (Accession NM_014035). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SBBI31. LOC124842 (Accession XM_064333) is another VGAM273 host target gene. LOC124842 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC124842, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124842 BINDING SITE, designated SEQ ID:37261, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15605] Another function of VGAM273 is therefore inhibition of LOC124842 (Accession XM_064333). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC124842. LOC138399 (Accession XM_059971) is another VGAM273 host target gene. LOC138399 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC138399, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC138399 BINDING SITE, designated SEQ ID:37131, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15606] Another function of VGAM273 is therefore inhibition of LOC138399 (Accession XM_059971). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC138399. LOC221814 (Accession XM_168226) is another VGAM273 host target gene. LOC221814 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC221814, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221814 BINDING SITE, designated SEQ ID:45090, to

the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15607] Another function of VGAM273 is therefore inhibition of LOC221814 (Accession XM_168226). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221814. LOC90317 (Accession XM_030892) is another VGAM273 host target gene. LOC90317 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90317 BINDING SITE, designated SEQ ID:31207, to the nucleotide sequence of VGAM273 RNA, herein designated VGAM RNA, also designated SEQ ID:2984.

[15608] Another function of VGAM273 is therefore inhibition of LOC90317 (Accession XM_030892). Accordingly, utilities of VGAM273 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90317. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 274 (VGAM274) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15609] VGAM274 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM274 was detected is described hereinabove with reference to Figs. 1–8.

[15610] VGAM274 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15611] VGAM274 gene encodes a VGAM274 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM274 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM274 precursor RNA is designated SEQ ID:260, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:260 is located at position 80659 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15612] VGAM274 precursor RNA folds onto itself, forming VGAM274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15613] An enzyme complex designated DICER COMPLEX, `dices` the VGAM274 folded precursor RNA into VGAM274 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM274 RNA is designated SEQ ID:2985, and is provided hereinbelow with reference to the sequence listing part.

[15614] VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM274 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM274 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15615] VGAM274 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM274 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM274 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15616] The complementary binding of VGAM274 RNA, herein designated VGAM RNA, to host target binding sites on VGAM274 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM274 host target RNA into VGAM274 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15617] It is appreciated that VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM274 host target genes. The mRNA of each one of this plurality of VGAM274 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM274 RNA, herein designated VGAM RNA, and which when bound by VGAM274 RNA causes inhibition of translation of respective one or more VGAM274 host target proteins.

[15618] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM274 gene, herein designated VGAM GENE, on one or more VGAM274 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15619] It is yet further appreciated that a function of VGAM274 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM274 correlate with, and may be deduced

from, the identity of the host target genes which VGAM274 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15620] Nucleotide sequences of the VGAM274 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM274 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM274 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM274 are further described hereinbelow with reference to Table 1.

[15621] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM274 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM274 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15622] As mentioned hereinabove with reference to Fig. 1, a function of VGAM274 gene, herein designated VGAM is inhibition of expression of VGAM274 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM274 correlate with, and may be deduced from, the identity of the target genes which VGAM274

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15623] SRB7 Suppressor of RNA Polymerase B Homolog (yeast) (SURB7, Accession NM_004264) is a VGAM274 host target gene. SURB7 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SURB7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SURB7 BINDING SITE, designated SEQ ID:10463, to the nucleotide sequence of VGAM274 RNA, herein designated VGAM RNA, also designated SEQ ID:2985.

[15624] A function of VGAM274 is therefore inhibition of SRB7 Suppressor of RNA Polymerase B Homolog (yeast) (SURB7, Accession NM_004264). Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SURB7. LOC221035 (Accession XM_167640) is another VGAM274 host target gene. LOC221035 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221035, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221035 BINDING SITE, designated SEQ ID:44745, to the nucleotide sequence of VGAM274 RNA, herein designated VGAM RNA, also designated SEQ ID:2985.

[15625] Another function of VGAM274 is therefore inhibition of LOC221035 (Accession XM_167640). Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221035. LOC221405 (Accession XM_168138) is another VGAM274 host target gene. LOC221405 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221405, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221405 BINDING SITE, designated SEQ ID:45065, to the nucleotide sequence of VGAM274 RNA, herein designated VGAM RNA, also designated SEQ ID:2985.

[15626] Another function of VGAM274 is therefore inhibition of LOC221405 (Accession XM_168138). Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC221405. LOC51701 (Accession NM_016231) is another VGAM274 host target gene. LOC51701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51701 BINDING SITE, designated SEQ ID:18344, to the nucleotide sequence of VGAM274 RNA, herein designated VGAM RNA, also designated SEQ ID:2985.

[15627] Another function of VGAM274 is therefore inhibition of LOC51701 (Accession NM_016231). Accordingly, utilities of VGAM274 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51701. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 275 (VGAM275) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15628] VGAM275 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM275 was detected is described hereinabove with reference to Figs. 1–8.

[15629] VGAM275 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15630] VGAM275 gene encodes a VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM275 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM275 precursor RNA is designated SEQ ID:261, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:261 is located at position 65605 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15631] VGAM275 precursor RNA folds onto itself, forming VGAM275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15632] An enzyme complex designated DICER COMPLEX, `dices` the VGAM275 folded precursor RNA into VGAM275 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 74%) nucleotide sequence of VGAM275 RNA is designated SEQ ID:2986, and is provided hereinbelow with reference to the sequence listing part.

[15633] VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM275 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15634] VGAM275 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM275 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM275 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15635] The complementary binding of VGAM275 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM275 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM275 host target RNA into VGAM275 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15636] It is appreciated that VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM275 host target genes. The mRNA of each one of this plurality of VGAM275 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM275 RNA, herein designated VGAM RNA, and which when bound by VGAM275 RNA causes inhibition of translation of respective one or more VGAM275 host target proteins.

[15637] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM275 gene, herein designated VGAM GENE, on one or more VGAM275 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15638] It is yet further appreciated that a function of VGAM275 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM275 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM275 correlate with, and may be deduced from, the identity of the host target genes which VGAM275 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15639] Nucleotide sequences of the VGAM275 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM275 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM275 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM275 are further described hereinbelow with reference to Table 1.

[15640] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM275 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM275 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15641] As mentioned hereinabove with reference to Fig. 1, a function of VGAM275 gene, herein designated VGAM is inhibition of expression of VGAM275 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM275 correlate with, and may be deduced from, the identity of the target genes which VGAM275 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15642] Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 5 (SLC9A5, Accession XM_007868) is a VGAM275 host target gene. SLC9A5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by SLC9A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A5 BINDING SITE, designated SEQ ID:30066, to the nucleotide sequence of VGAM275 RNA, herein designated VGAM RNA, also designated SEQ ID:2986.

[15643] A function of VGAM275 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 5 (SLC9A5, Accession XM_007868). Accordingly, utilities of VGAM275 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A5. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 276 (VGAM276) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15644] VGAM276 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM276 was detected is described hereinabove with reference to Figs. 1–8.

[15645] VGAM276 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15646] VGAM276 gene encodes a VGAM276 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM276 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM276 precursor RNA is designated SEQ ID:262, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:262 is located at position 19006 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15647] VGAM276 precursor RNA folds onto itself, forming VGAM276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15648] An enzyme complex designated DICER COMPLEX, `dices` the VGAM276 folded precursor RNA into VGAM276 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 46%) nucleotide sequence of VGAM276 RNA is designated SEQ ID:2987, and is provided hereinbelow with reference to the sequence listing part.

[15649] VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM276 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15650] VGAM276 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM276 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM276 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15651] The complementary binding of VGAM276 RNA, herein designated VGAM RNA, to host target binding sites on VGAM276 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM276 host tar-

get RNA into VGAM276 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15652] It is appreciated that VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM276 host target genes. The mRNA of each one of this plurality of VGAM276 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM276 RNA, herein designated VGAM RNA, and which when bound by VGAM276 RNA causes inhibition of translation of respective one or more VGAM276 host target proteins.

[15653] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM276 gene, herein designated VGAM GENE, on one or more VGAM276 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15654] It is yet further appreciated that a function of VGAM276 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM276 correlate with, and may be deduced from, the identity of the host target genes which VGAM276 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15655] Nucleotide sequences of the VGAM276 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM276 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM276 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM276 are further

described hereinbelow with reference to Table 1.

[15656] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM276 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM276 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15657] As mentioned hereinabove with reference to Fig. 1, a function of VGAM276 gene, herein designated VGAM is inhibition of expression of VGAM276 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM276 correlate with, and may be deduced from, the identity of the target genes which VGAM276 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15658] Fibroblast Growth Factor 5 (FGF5, Accession NM_004464) is a VGAM276 host target gene. FGF5 BINDING SITE1 and FGF5 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FGF5, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FGF5 BINDING SITE1 and FGF5 BINDING SITE2, designated SEQ ID:10773 and SEQ ID:27000 respectively, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15659] A function of VGAM276 is therefore inhibition of Fibroblast Growth Factor 5 (FGF5, Accession NM_004464), a gene which induces transformation and may regulate neuronal differentiation. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FGF5. The function of FGF5 has been established by previous studies. Zhan et al. (1988) identified a fifth oncogene related to fibroblast growth factors and termed it FGF5. The other four are FGFA (OMIM Ref. No. 131220), FGFB (OMIM Ref. No. 134920), INT2 (OMIM Ref. No. 164950), and HST (OMIM Ref. No. 164980). FGF5 was discovered when it acquired transforming potential by a DNA rearrangement accompanying transfection of NIH 3T3 cells with human tumor DNA. Two regions of the FGF5 sequence, containing 122 of its 267 amino acid residues, were 40 to 50% homologous to the sequences of the 4 other members of the FGF oncogene family. FGF5, furthermore, was found to have a 3-exon structure typical for members of this family. FGF5

was found to be expressed in neonatal brain and in 3 of 13 human tumor cell lines examined. Nguyen et al. (1988) mapped FGF5 to 4q21 by in situ hybridization. Thus, it is not in the same cluster as the related HST and INT2 genes, which are coamplified in some tumor cells and were found by Nguyen et al. (1988), using pulsed field gel analysis, to be separated by only 40 kb. By polymerase chain reaction (PCR) amplification of target sequences in DNAs from somatic cell hybrids, Dionne et al. (1990) mapped the FGF5 gene to chromosome 4. By in situ chromosomal hybridization, Mattei et al. (1992) demonstrated that the corresponding gene in the mouse is on chromosome 5. Hebert et al. (1994) found that mice homozygous for a null allele of the *Fgf5* gene, produced by gene targeting in embryonic stem cells, have abnormally long hair. This phenotype appeared identical to that of mice homozygous for the spontaneous mutation 'angora' (*go*). The transgenic mutant and the '*go*' mutant failed to complement one another, and exon 1 of *Fgf5* was found to be deleted in DNA from *go* homozygotes. Expression of *Fgf5* is detected in hair follicles from wildtype mice and is localized to the outer root sheath during the anagen VI phase of the hair growth cycle. The findings were interpreted as evi-

dence that FGF5 functions as an inhibitor of hair elongation, thus identifying a molecule whose normal function is apparently to regulate one step in the progression of the follicle through the hair growth cycle. It will be of interest to search for mutations in the FGF5 gene in hypertrichosis universalis (145700, 145701) as well as in other forms of hypertrichosis such as hairy elbows (OMIM Ref. No. 139600).

[15660] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15661] Zhan, X.; Bates, B.; Hu, X.; Goldfarb, M. : The human FGF-5 oncogene encodes a novel protein related to fibroblast growth factors. *Molec. Cell. Biol.* 8: 3487-3495, 1988. ; and

[15662] Hebert, J. M.; Rosenquist, T.; Gotz, J.; Martin, G. R. : FGF5 as a regulator of the hair growth cycle: evidence from targeted and spontaneous mutations. *Cell* 78: 1017-1025, 1994.

[15663] Further studies establishing the function and utilities of FGF5 are found in John Hopkins OMIM database record ID 165190, and in cited publications numbered 698-699, 17 and 700-701 listed in the bibliography section hereinbe-

low, which are also hereby incorporated by reference. Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM_009699) is another VGAM276 host target gene. NRIP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NRIP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NRIP1 BINDING SITE, designated SEQ ID:30118, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15664] Another function of VGAM276 is therefore inhibition of Nuclear Receptor Interacting Protein 1 (NRIP1, Accession XM_009699), a gene which modulates transcriptional activation by the estrogen receptor. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NRIP1. The function of NRIP1 has been established by previous studies. Cavailles et al. (1995) identified the receptor-interacting protein 140 (OMIM Ref. No. RIP140) by virtue of its direct association with a transcriptional activation domain of the estrogen receptor (ESR; 133430) in the presence of estrogen; by fluorescence in situ hybridization

with a cDNA clone, they mapped the gene to 21q11. Katsanis et al. (1998) used hybrids, YACs, and PACs to place the RIP140 gene on the physical map of chromosome 21; 21q11 is a gene-poor region.

[15665] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15666] Cavailles, V.; Dauvois, S.; Horset, L. F.; Lopez, G.; Hoare, S.; Kushner, P. J.; Parker, M. G. : Nuclear factor RIP140 modulates transcriptional activation by the estrogen receptor. EMBO J. 14: 3741–3751, 1995. ; and

[15667] Katsanis, N.; Ives, J. H.; Groet, J.; Nizetic, D.; Fisher, E. M. C. : Localisation of receptor interacting protein 140 (RIP140) within 100 kb of D21S13 on 21q11, a gene-poor region of t.

[15668] Further studies establishing the function and utilities of NRIP1 are found in John Hopkins OMIM database record ID 602490, and in cited publications numbered 1036–1037 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM_004571) is another VGAM276 host target gene. PKNOX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by PKNOX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PKNOX1 BINDING SITE, designated SEQ ID:10913, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15669] Another function of VGAM276 is therefore inhibition of PBX/knotted 1 Homeobox 1 (PKNOX1, Accession NM_004571), a gene which may regulate gene expression and control cell differentiation. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PKNOX1. The function of PKNOX1 has been established by previous studies. As part of developing a transcript map of human chromosome 21, Chen et al. (1997) used exon trapping to identify portions of genes from chromosome 21-specific cosmids. They identified a trapped exon that is identical to a region of the human expressed sequence tag (EST) L12425. Using the exon and EST as probes, they screened human fetal brain and kidney cDNA libraries and cloned the corresponding gene, which encodes a homeodomain-containing polypeptide of 436 amino acids. Chen et al.

(1997) used the EST as a probe for Northern analysis and detected transcripts of 2.5 and 5 kb in every human tissue examined, including heart, brain and brain subregions, placenta, lung, liver, muscle, and several fetal tissues. The gene, designated PBX/knotted-1 homeo box-1 (OMIM Ref. No. PKNOX1), has a homeodomain closely related to those of the mammalian PBX family (such as mouse Meis1) and the plant knotted-1 family (involved in plant development). Chen et al. (1997) used PCR amplification, hybridization, and genetic linkage analysis to map PKNOX1 to 21q22.3 between markers D21S212 and D21S25 on YAC350F7. By fluorescence in situ hybridization, Berthelsen et al. (1998) mapped the PKNOX1 gene to human chromosome 21q22.3 and mouse chromosome 17B/C.

[15670] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15671] Berthelsen, J.; Viggiano, L.; Schulz, H.; Ferretti, E.; Gonzalez, G. G.; Rocchi, M.; Blasi, F. : PKNOX1, a gene encoding PREP1, a new regulator of Pbx activity, maps on human chromosome 21q22.3 and murine chromosome 17B/C. Genomics 47: 323-324, 1998. ; and

[15672] Chen, H.; Rossier, C.; Nakamura, Y.; Lynn, A.; Chakravarti, A.; Antonarakis, S. E. : Cloning of a novel homeobox-containing gene, PKNOX1, and mapping to human chromosome 21q22.3. Genomi.

[15673] Further studies establishing the function and utilities of PKNOX1 are found in John Hopkins OMIM database record ID 602100, and in cited publications numbered 8527–8528 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. TIA1 Cytotoxic Granule-associated RNA Binding Protein (TIA1, Accession NM_022173) is another VGAM276 host target gene. TIA1 BINDING SITE1 and TIA1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TIA1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TIA1 BINDING SITE1 and TIA1 BINDING SITE2, designated SEQ ID:22734 and SEQ ID:22559 respectively, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15674] Another function of VGAM276 is therefore inhibition of TIA1 Cytotoxic Granule-associated RNA Binding Protein

(TIA1, Accession NM_022173), a gene which possesses nucleolytic activity against cytotoxic lymphocyte target cells. Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TIA1. The function of TIA1 has been established by previous studies. Cytolytic lymphocytes (CTLs) are characterized by their inclusion of cytoplasmic granules containing effector molecules that can mediate target cell death. One mechanism of lymphocyte-mediated killing is the induction of target cell apoptosis. Central to this autolytic pathway is the activation of an endogenous endonuclease that degrades target cell DNA. TIA1 is a 15-kD cytoplasmic granule-associated protein whose expression is restricted to CTLs and natural killer cells (Anderson et al., 1990). Upon activation with mitogens or with antibodies reactive with the T-cell receptor complex, the expression of TIA1 greatly increases and 28-, 40-, and 53-kD forms of the protein are induced. Tian et al. (1991) described the cDNA cloning and functional characterization of 2 TIA1 isoforms. By immunoscreening a cytolytic T-cell cDNA expression library with a monoclonal antibody against TIA1, they isolated a 1.6-kb TIA1 cDNA encoding a deduced 146-amino acid protein,

referred to as rp15-TIA1, that has an apparent molecular mass of 15 kD by SDS-PAGE. Using the 1.6-kb cDNA to screen a phytohemagglutinin-activated T-cell cDNA library, the authors isolated a 2.2-kb cDNA encoding a deduced 375-amino acid protein, referred to as rp40-TIA1, that has an apparent molecular mass of 40 kD by SDS-PAGE. The 1.6-kb cDNA is identical in sequence to the last 1,618 bp of the 2.2-kb cDNA. The rp40-TIA1 protein contains 3 RNA-binding domains, each with 2 ribonucleoprotein consensus octapeptide sequences, at the N terminus, and a glutamine-rich domain and a lysosomal membrane-targeting motif at the C terminus; the rp15-TIA1 protein contains the glutamine-rich domain and the lysosomal membrane-targeting motif. Tian et al. (1991) suggested that the 15-kD TIA1 isoform may be derived from the 40-kD isoform by proteolytic processing and showed that peripheral blood lymphocytes express a protease capable of specifically cleaving rp40-TIA1, resulting in the release of its 15-kD C terminus. The authors demonstrated that TIA1 is a nucleic acid-binding protein that preferentially recognizes poly(A) homopolymers, and induces DNA fragmentation in permeabilized thymocytes. They suggested that TIA1 may be involved in the induc-

tion of apoptosis in CTL targets. Northern blot analysis detected 2.7- and 4.0-kb TIA1 transcripts in lymphocytes and 1.7-, 2.2-, 2.7-, and 4.0-kb TIA1 transcripts in a cytotoxic T-cell clone. Forch et al. (2000) reported that the apoptosis-promoting protein TIA1 regulates alternative pre-mRNA splicing of the *Drosophila* male-specific lethal-2 gene (*Msl2*; OMIM Ref. No. 604880) and of the human apoptotic gene *FAS* (*TNFRSF6*; 134637). TIA1 associates selectively with pre-mRNAs that contain 5-prime splice sites followed by U-rich sequences. TIA1 binding to the U-rich stretches facilitates 5-prime splice site recognition by U1 snRNP (see OMIM Ref. No. 180740). This activity is critical for activation of the weak 5-prime splice site of *Msl2* and for modulating the choice of splice site partner in *FAS*. Structural and functional similarities with the *S. cerevisiae* splicing factor *Nam8* suggest striking evolutionary conservation of a mechanism of pre-mRNA splicing regulation that controls biologic processes as diverse as meiosis in yeast, dosage compensation in fruit flies, or programmed cell death in humans.

[15675] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [15676] Tian, Q.; Streuli, M.; Saito, H.; Schlossman, S. F.; Anderson, P. : A polyadenylate binding protein localized to the granules of cytolytic lymphocytes induces DNA fragmentation in target cells. *Cell* 67: 629–639, 1991. ; and
- [15677] Forch, P.; Puig, O.; Kedersha, N.; Martinez, C.; Granneman, S.; Seraphin, B.; Anderson, P.; Valcarcel, J. : The apoptosis-promoting factor TIA-1 is a regulator of alternative pre-mRNA s.
- [15678] Further studies establishing the function and utilities of TIA1 are found in John Hopkins OMIM database record ID 603518, and in cited publications numbered 8669–8672 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZp434A2417 (Accession XM_038526) is another VGAM276 host target gene. DKFZp434A2417 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434A2417, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434A2417 BINDING SITE, designated SEQ ID:32862, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15679] Another function of VGAM276 is therefore inhibition of DKFZp434A2417 (Accession XM_038526). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434A2417. DKFZp761B1514 (Accession NM_032288) is another VGAM276 host target gene. DKFZp761B1514 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761B1514, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp761B1514 BINDING SITE, designated SEQ ID:26046, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15680] Another function of VGAM276 is therefore inhibition of DKFZp761B1514 (Accession NM_032288). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761B1514. FLJ20136 (Accession NM_017684) is another VGAM276 host target gene. FLJ20136 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20136, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20136 BINDING SITE, designated SEQ ID:19228, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15681] Another function of VGAM276 is therefore inhibition of FLJ20136 (Accession NM_017684). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20136. KIAA0410 (Accession NM_014778) is another VGAM276 host target gene. KIAA0410 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0410, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0410 BINDING SITE, designated SEQ ID:16617, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15682] Another function of VGAM276 is therefore inhibition of KIAA0410 (Accession NM_014778). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0410. KIAA1908 (Accession XM_055834) is another VGAM276 host target gene. KIAA1908 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1908, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1908 BINDING SITE, designated SEQ ID:36329, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15683] Another function of VGAM276 is therefore inhibition of KIAA1908 (Accession XM_055834). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1908. Paternally Expressed 10 (PEG10, Accession NM_015068) is another VGAM276 host target gene. PEG10 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PEG10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PEG10 BINDING SITE, designated SEQ

ID:17427, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15684] Another function of VGAM276 is therefore inhibition of Paternally Expressed 10 (PEG10, Accession NM_015068). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PEG10. PHD Finger Protein 7 (PHF7, Accession NM_016483) is another VGAM276 host target gene. PHF7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PHF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHF7 BINDING SITE, designated SEQ ID:18580, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15685] Another function of VGAM276 is therefore inhibition of PHD Finger Protein 7 (PHF7, Accession NM_016483). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHF7. Proline-rich Gla (G-carboxyglutamic acid) Polypeptide 1 (PRRG1, Accession NM_000950) is an-

other VGAM276 host target gene. PRRG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRRG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRRG1 BINDING SITE, designated SEQ ID:6651, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15686] Another function of VGAM276 is therefore inhibition of Proline-rich Gla (G-carboxyglutamic acid) Polypeptide 1 (PRRG1, Accession NM_000950). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRRG1. LOC129198 (Accession XM_072197) is another VGAM276 host target gene. LOC129198 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC129198, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC129198 BINDING SITE, designated SEQ ID:37463, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA,

also designated SEQ ID:2987.

[15687] Another function of VGAM276 is therefore inhibition of LOC129198 (Accession XM_072197). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC129198. LOC145719 (Accession XM_096848) is another VGAM276 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40571, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15688] Another function of VGAM276 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM276 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145720, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40561, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15689] Another function of VGAM276 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145720. LOC158295 (Accession XM_098915) is another VGAM276 host target gene. LOC158295 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158295 BINDING SITE, designated SEQ ID:41938, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15690] Another function of VGAM276 is therefore inhibition of LOC158295 (Accession XM_098915). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC158295. LOC197114 (Accession XM_116987) is another VGAM276 host target gene. LOC197114 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197114 BINDING SITE, designated SEQ ID:43185, to the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15691] Another function of VGAM276 is therefore inhibition of LOC197114 (Accession XM_116987). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197114. LOC197117 (Accession XM_116989) is another VGAM276 host target gene. LOC197117 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC197117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197117 BINDING SITE, designated SEQ ID:43194, to

the nucleotide sequence of VGAM276 RNA, herein designated VGAM RNA, also designated SEQ ID:2987.

[15692] Another function of VGAM276 is therefore inhibition of LOC197117 (Accession XM_116989). Accordingly, utilities of VGAM276 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197117. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 277 (VGAM277) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15693] VGAM277 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM277 was detected is described hereinabove with reference to Figs. 1–8.

[15694] VGAM277 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15695] VGAM277 gene encodes a VGAM277 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM277 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM277 precursor RNA is designated SEQ ID:263, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:263 is located at position 54634 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15696] VGAM277 precursor RNA folds onto itself, forming VGAM277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15697] An enzyme complex designated DICER COMPLEX, `dices` the VGAM277 folded precursor RNA into VGAM277 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM277 RNA is designated SEQ ID:2988, and is provided hereinbelow with reference to the sequence listing part.

[15698] VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM277 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15699] VGAM277 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM277 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM277 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15700] The complementary binding of VGAM277 RNA, herein designated VGAM RNA, to host target binding sites on VGAM277 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM277 host target RNA into VGAM277 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15701] It is appreciated that VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM277 host target genes. The mRNA of each one of this plurality of VGAM277 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM277 RNA, herein designated VGAM RNA, and which when bound by VGAM277 RNA causes inhibition of translation of respective one or more VGAM277 host target proteins.

[15702] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM277 gene, herein designated VGAM GENE, on one or more VGAM277 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[15703] It is yet further appreciated that a function of VGAM277 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM277 correlate with, and may be deduced from, the identity of the host target genes which VGAM277 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15704] Nucleotide sequences of the VGAM277 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM277 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM277 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM277 are further described hereinbelow with reference to Table 1.

[15705] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM277 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM277 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15706] As mentioned hereinabove with reference to Fig. 1, a function of VGAM277 gene, herein designated VGAM is inhibition of expression of VGAM277 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM277 correlate with, and may be deduced from, the identity of the target genes which VGAM277 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15707] DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession NM_004412) is a VGAM277 host target gene. DNMT2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNMT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT2 BINDING SITE, designated SEQ ID:10673, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15708] A function of VGAM277 is therefore inhibition of DNA (cytosine-5-)-methyltransferase 2 (DNMT2, Accession

NM_004412), a gene which may mark specific sequences in the genome . Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT2. The function of DNMT2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM177. ELL (Accession NM_006532) is another VGAM277 host target gene. ELL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELL BINDING SITE, designated SEQ ID:13281, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15709] Another function of VGAM277 is therefore inhibition of ELL (Accession NM_006532). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELL. Mitogen-activated Protein Kinase Kinase Kinase 7 Interacting Protein 2 (MAP3K7IP2, Accession NM_015093) is another VGAM277 host target gene. MAP3K7IP2 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP3K7IP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K7IP2 BINDING SITE, designated SEQ ID:17489, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15710] Another function of VGAM277 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 7 Inter-acting Protein 2 (MAP3K7IP2, Accession NM_015093). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K7IP2. Mitochondrial Ribosomal Protein L49 (MRPL49, Accession XM_045499) is another VGAM277 host target gene. MRPL49 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL49, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MRPL49 BINDING SITE, designated SEQ ID:34477, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA,

also designated SEQ ID:2988.

[15711] Another function of VGAM277 is therefore inhibition of Mitochondrial Ribosomal Protein L49 (MRPL49, Accession XM_045499). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL49. Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_007331) is another VGAM277 host target gene. WHSC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WHSC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE, designated SEQ ID:14248, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15712] Another function of VGAM277 is therefore inhibition of Wolf-Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_007331), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases

and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200.CGI-203 (Accession NM_020408) is another VGAM277 host target gene. CGI-203 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by CGI-203, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CGI-203 BINDING SITE, designated SEQ ID:21676, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15713] Another function of VGAM277 is therefore inhibition of CGI-203 (Accession NM_020408). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CGI-203. CCR4-NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779) is another VGAM277 host target gene. CNOT8 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CNOT8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of CNOT8 BINDING SITE, designated SEQ ID:11178, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15714] Another function of VGAM277 is therefore inhibition of CCR4–NOT Transcription Complex, Subunit 8 (CNOT8, Accession NM_004779). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNOT8. FLJ21709 (Accession XM_085480) is another VGAM277 host target gene. FLJ21709 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ21709, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21709 BINDING SITE, designated SEQ ID:38173, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15715] Another function of VGAM277 is therefore inhibition of FLJ21709 (Accession XM_085480). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21709.

FLJ21939 (Accession NM_022461) is another VGAM277 host target gene. FLJ21939 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21939, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21939 BINDING SITE, designated SEQ ID:22802, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15716] Another function of VGAM277 is therefore inhibition of FLJ21939 (Accession NM_022461). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21939. LOC152503 (Accession XM_098238) is another VGAM277 host target gene. LOC152503 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC152503, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152503 BINDING SITE, designated SEQ ID:41519, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA,

also designated SEQ ID:2988.

[15717] Another function of VGAM277 is therefore inhibition of LOC152503 (Accession XM_098238). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152503. LOC152897 (Accession XM_087555) is another VGAM277 host target gene. LOC152897 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152897, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152897 BINDING SITE, designated SEQ ID:39328, to the nucleotide sequence of VGAM277 RNA, herein designated VGAM RNA, also designated SEQ ID:2988.

[15718] Another function of VGAM277 is therefore inhibition of LOC152897 (Accession XM_087555). Accordingly, utilities of VGAM277 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152897. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 278 (VGAM278) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15719] VGAM278 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM278 was detected is described hereinabove with reference to Figs. 1–8.

[15720] VGAM278 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15721] VGAM278 gene encodes a VGAM278 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM278 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM278 precursor RNA is designated SEQ ID:264, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:264 is located at position 17046 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15722] VGAM278 precursor RNA folds onto itself, forming

VGAM278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15723] An enzyme complex designated DICER COMPLEX, `dices` the VGAM278 folded precursor RNA into VGAM278 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 86%) nucleotide sequence of VGAM278 RNA is designated SEQ ID:2989, and is provided hereinbelow with reference to the sequence listing part.

[15724] VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM278 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15725] VGAM278 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM278 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM278 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15726] The complementary binding of VGAM278 RNA, herein designated VGAM RNA, to host target binding sites on VGAM278 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM278 host target RNA into VGAM278 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15727] It is appreciated that VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM278 host target genes. The mRNA of each one of this plurality of VGAM278 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM278 RNA, herein designated VGAM RNA, and which when bound by VGAM278 RNA causes inhibition of translation of respective one or more VGAM278 host target proteins.

[15728] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM278 gene, herein designated VGAM GENE, on one or more VGAM278 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15729] It is yet further appreciated that a function of VGAM278 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM278 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM278 correlate with, and may be deduced from, the identity of the host target genes which

VGAM278 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15730] Nucleotide sequences of the VGAM278 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM278 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM278 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM278 are further described hereinbelow with reference to Table 1.

[15731] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM278 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM278 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15732] As mentioned hereinabove with reference to Fig. 1, a function of VGAM278 gene, herein designated VGAM is inhibition of expression of VGAM278 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM278 correlate with, and may be deduced from, the identity of the target genes which VGAM278 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[15733] Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM_056815) is a VGAM278 host target gene. PDE4D BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PDE4D, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE4D BINDING SITE, designated SEQ ID:36426, to the nucleotide sequence of VGAM278 RNA, herein designated VGAM RNA, also designated SEQ ID:2989.

[15734] A function of VGAM278 is therefore inhibition of Phosphodiesterase 4D, CAMP-specific (phosphodiesterase E3 dunce homolog, *Drosophila*) (PDE4D, Accession XM_056815), a gene which has similarity to *Drosophila* dnc, which is the affected protein in learning and memory mutant dunce. Accordingly, utilities of VGAM278 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE4D. The function of PDE4D and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM180. Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621) is another VGAM278 host target gene. TRPC6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by TRPC6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPC6 BINDING SITE, designated SEQ ID:10977, to the nucleotide sequence of VGAM278 RNA, herein designated VGAM RNA, also designated SEQ ID:2989.

[15735] Another function of VGAM278 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily C, Member 6 (TRPC6, Accession NM_004621), a gene which has calcium channel activity. Accordingly, utilities of VGAM278 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPC6. The function of TRPC6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 279 (VGAM279) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15736] VGAM279 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM279 was detected is described hereinabove with reference to Figs. 1–8.

[15737] VGAM279 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15738] VGAM279 gene encodes a VGAM279 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM279 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM279 precursor RNA is designated SEQ ID:265, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:265 is located at position 12207 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15739] VGAM279 precursor RNA folds onto itself, forming VGAM279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15740] An enzyme complex designated DICER COMPLEX, `dices` the VGAM279 folded precursor RNA into VGAM279 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM279 RNA is designated SEQ ID:2990, and is provided hereinbelow with reference to the sequence listing part.

[15741] VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM279 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM279 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15742] VGAM279 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM279 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM279 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15743] The complementary binding of VGAM279 RNA, herein designated VGAM RNA, to host target binding sites on VGAM279 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM279 host target RNA into VGAM279 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15744] It is appreciated that VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM279 host target genes. The mRNA of each one of this plurality of VGAM279 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM279 RNA, herein designated VGAM RNA, and which when bound by VGAM279 RNA causes inhibition of translation of respective one or more VGAM279 host target proteins.

[15745] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM279 gene, herein designated VGAM GENE, on one or more VGAM279 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15746] It is yet further appreciated that a function of VGAM279 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM279 correlate with, and may be deduced

from, the identity of the host target genes which VGAM279 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15747] Nucleotide sequences of the VGAM279 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM279 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM279 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM279 are further described hereinbelow with reference to Table 1.

[15748] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM279 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM279 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15749] As mentioned hereinabove with reference to Fig. 1, a function of VGAM279 gene, herein designated VGAM is inhibition of expression of VGAM279 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM279 correlate with, and may be deduced from, the identity of the target genes which VGAM279

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15750] DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397) is a VGAM279 host target gene. DDX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DDX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DDX6 BINDING SITE, designated SEQ ID:10647, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15751] A function of VGAM279 is therefore inhibition of DEAD/H (Asp-Glu-Ala-Asp/His) Box Polypeptide 6 (RNA helicase, 54kDa) (DDX6, Accession NM_004397), a gene which is putative RNA helicases. Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DDX6. The function of DDX6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Engulfment and Cell Motility 2 (ced-12 ho-

molog, *C. elegans*) (ELMO2, Accession NM_133171) is another VGAM279 host target gene. ELMO2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ELMO2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ELMO2 BINDING SITE, designated SEQ ID:28395, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15752] Another function of VGAM279 is therefore inhibition of Engulfment and Cell Motility 2 (*ced-12* homolog, *C. elegans*) (ELMO2, Accession NM_133171). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ELMO2. Hepatocyte Growth Factor (hepatopoietin A; scatter factor) (HGF, Accession XM_168542) is another VGAM279 host target gene. HGF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HGF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HGF BINDING SITE, designated

SEQ ID:45230, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15753] Another function of VGAM279 is therefore inhibition of Hepatocyte Growth Factor (hepapoietin A; scatter factor) (HGF, Accession XM_168542), a gene which may be required for normal embryonic development; strongly similar to murine Hgf, has kringle domains. Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HGF. The function of HGF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM174. Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM_085082) is another VGAM279 host target gene. ARHGAP5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGAP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP5 BINDING SITE, designated SEQ ID:37822, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ

ID:2990.

[15754] Another function of VGAM279 is therefore inhibition of Rho GTPase Activating Protein 5 (ARHGAP5, Accession XM_085082). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP5. DKFZP434P0721 (Accession XM_033181) is another VGAM279 host target gene. DKFZP434P0721 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434P0721, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434P0721 BINDING SITE, designated SEQ ID:31872, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15755] Another function of VGAM279 is therefore inhibition of DKFZP434P0721 (Accession XM_033181). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434P0721. FLJ13189 (Accession NM_024882) is another VGAM279 host target gene. FLJ13189 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by FLJ13189, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13189 BINDING SITE, designated SEQ ID:24334, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15756] Another function of VGAM279 is therefore inhibition of FLJ13189 (Accession NM_024882). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13189. FLJ20456 (Accession NM_017831) is another VGAM279 host target gene. FLJ20456 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20456, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20456 BINDING SITE, designated SEQ ID:19494, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15757] Another function of VGAM279 is therefore inhibition of FLJ20456 (Accession NM_017831). Accordingly, utilities of

VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20456. FLJ20695 (Accession NM_017929) is another VGAM279 host target gene. FLJ20695 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ20695, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20695 BINDING SITE, designated SEQ ID:19613, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15758] Another function of VGAM279 is therefore inhibition of FLJ20695 (Accession NM_017929). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20695. KIAA1754 (Accession XM_032587) is another VGAM279 host target gene. KIAA1754 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1754, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1754 BINDING SITE,

designated SEQ ID:31682, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15759] Another function of VGAM279 is therefore inhibition of KIAA1754 (Accession XM_032587). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1754. Nucleosome Assembly Protein 1-like 2 (NAP1L2, Accession NM_021963) is another VGAM279 host target gene. NAP1L2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAP1L2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAP1L2 BINDING SITE, designated SEQ ID:22497, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15760] Another function of VGAM279 is therefore inhibition of Nucleosome Assembly Protein 1-like 2 (NAP1L2, Accession NM_021963). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAP1L2. LOC150159

(Accession NM_139173) is another VGAM279 host target gene. LOC150159 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150159, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150159 BINDING SITE, designated SEQ ID:29182, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15761] Another function of VGAM279 is therefore inhibition of LOC150159 (Accession NM_139173). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150159. LOC164714 (Accession XM_104657) is another VGAM279 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42180, to the nucleotide sequence of VGAM279 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2990.

[15762] Another function of VGAM279 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC196485 (Accession XM_113731) is another VGAM279 host target gene. LOC196485 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC196485, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC196485 BINDING SITE, designated SEQ ID:42383, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15763] Another function of VGAM279 is therefore inhibition of LOC196485 (Accession XM_113731). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC196485. LOC199858 (Accession XM_114040) is another VGAM279 host target gene. LOC199858 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199858, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42636, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15764] Another function of VGAM279 is therefore inhibition of LOC199858 (Accession XM_114040). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC202986 (Accession XM_117489) is another VGAM279 host target gene. LOC202986 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC202986, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC202986 BINDING SITE, designated SEQ ID:43474, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15765] Another function of VGAM279 is therefore inhibition of LOC202986 (Accession XM_117489). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC202986. LOC222060 (Accession XM_168427) is another VGAM279 host target gene. LOC222060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222060 BINDING SITE, designated SEQ ID:45159, to the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15766] Another function of VGAM279 is therefore inhibition of LOC222060 (Accession XM_168427). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222060. LOC222160 (Accession XM_168431) is another VGAM279 host target gene. LOC222160 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222160, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222160 BINDING SITE, designated SEQ ID:45168, to

the nucleotide sequence of VGAM279 RNA, herein designated VGAM RNA, also designated SEQ ID:2990.

[15767] Another function of VGAM279 is therefore inhibition of LOC222160 (Accession XM_168431). Accordingly, utilities of VGAM279 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222160. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 280 (VGAM280) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15768] VGAM280 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM280 was detected is described hereinabove with reference to Figs. 1–8.

[15769] VGAM280 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15770] VGAM280 gene encodes a VGAM280 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM280 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM280 precursor RNA is designated SEQ ID:266, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:266 is located at position 110345 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15771] VGAM280 precursor RNA folds onto itself, forming VGAM280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15772] An enzyme complex designated DICER COMPLEX, `dices` the VGAM280 folded precursor RNA into VGAM280 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM280 RNA is designated SEQ ID:2991, and is provided hereinbelow with reference to the sequence listing part.

[15773] VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM280 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15774] VGAM280 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM280 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM280 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15775] The complementary binding of VGAM280 RNA, herein designated VGAM RNA, to host target binding sites on VGAM280 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM280 host target RNA into VGAM280 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15776] It is appreciated that VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM280 host target genes. The mRNA of each one of this plurality of VGAM280 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM280 RNA, herein designated VGAM RNA, and which when bound by VGAM280 RNA causes inhibition of translation of respective one or more VGAM280 host target proteins.

[15777] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM280 gene, herein designated VGAM GENE, on one or more VGAM280 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[15778] It is yet further appreciated that a function of VGAM280 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM280 correlate with, and may be deduced from, the identity of the host target genes which VGAM280 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15779] Nucleotide sequences of the VGAM280 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM280 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM280 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM280 are further described hereinbelow with reference to Table 1.

[15780] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM280 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM280 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15781] As mentioned hereinabove with reference to Fig. 1, a function of VGAM280 gene, herein designated VGAM is inhibition of expression of VGAM280 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM280 correlate with, and may be deduced from, the identity of the target genes which VGAM280 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15782] DNA (cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM_006892) is a VGAM280 host target gene. DNMT3B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DNMT3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNMT3B BINDING SITE, designated SEQ ID:13764, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15783] A function of VGAM280 is therefore inhibition of DNA

(cytosine-5-)-methyltransferase 3 Beta (DNMT3B, Accession NM_006892), a gene which is required for genome wide de novo methylation. Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNMT3B. The function of DNMT3B has been established by previous studies. Ehrlich et al. (2001) performed microarray expression analysis on B-cell lymphoblastoid cell lines from 5 ICF patients with diverse DNMT3B mutations and on control lymphoblastoid cell lines. They employed oligonucleotide arrays for approximately 5600 different genes, 510 of which showed a lymphoid lineage-restricted expression pattern among several different lineages tested. A set of 32 genes, half of which are thought to play a role in immune function, had consistent and significant ICF-specific changes in RNA levels. ICF-specific increases in immunoglobulin (Ig) heavy constant mu- and delta-RNA and cell surface IgM and IgD, decreases in Ig-gamma and Ig-alpha RNA, and surface IgG and IgA suggested inhibition of the later steps of lymphocyte maturation. ICF-specific increases were seen in RNA for RGS1 (OMIM Ref. No. 600323), a B-cell specific inhibitor of G-protein signaling implicated in negative regulation of B-cell migra-

tion, and in RNA for the proapoptotic protein kinase C ϵ gene (OMIM Ref. No. 605437). ICF-associated decreases were observed in RNAs encoding proteins involved in activation, migration, or survival of lymphoid cells, namely, transcription factor negative regulator ID3 (OMIM Ref. No. 600277), the enhancer-binding MEF2C (OMIM Ref. No. 600662), the iron regulatory TFRC (OMIM Ref. No. 190010), integrin beta-7 (ITGB7; 147559), the stress protein heme oxygenase (HMOX1; 141250), and the lymphocyte-specific tumor necrosis factor receptor family members 7 and 17 (TNFRSF7, 186711; TNFRSF17, 109545). No differences in promoter methylation were seen between ICF and normal lymphoblastoid cell lines for 3 ICF upregulated genes and 1 downregulated gene by a quantitative methylation assay. The authors hypothesized that DNMT3B mutations in the ICF syndrome may cause lymphogenesis-associated gene dysregulation by indirect effects on gene expression that interfere with normal lymphocyte signaling, maturation, and migration. Shirohzu et al. (2002) reported 3 Japanese cases of ICF syndrome from 2 unrelated families. All patients had typical facial dysmorphism and IgA deficiency, but none of them had apparent mental retardation. Cytogenetic analysis of pe-

peripheral blood lymphocytes showed chromosomal abnormalities, including multiradial configurations and a stretching of the pericentromeric heterochromatin of chromosomes 1 and 16. Hypomethylation of classical satellite-2 DNA was also observed. Three mutations in DNMT3B were found. One patient was a compound heterozygote for a gln42-to-ter (Q42X; 602900.0011) and an arg832-to-gln (R832Q; 602900.0012) mutation. The 2 patients from the second family were both homozygous for a ser282-to-pro (S282P; 602900.0013) mutation. Animal model experiments lend further support to the function of DNMT3B. Okano et al. (1999) generated mice with targeted disruption of the Dnmt3a and Dnmt3b genes. Inactivation of both genes blocked de novo methylation in embryonic stem cells and early embryos but had no effect on maintenance of imprinted methylation patterns.

Dnmt3a $-/-$ mice developed to term and appeared to be normal at birth. However, most homozygous mutant mice became runted and died at about 4 weeks of age. In contrast, no viable Dnmt3b $-/-$ mice were recovered at birth. Dissection of embryos at different stages of development revealed that Dnmt3b $-/-$ embryos had multiple developmental defects, including growth impairment and rostral

neural tube defects with variable severity at later stages of development, though most of them appeared to develop normally before E9.5. Dnmt3a and Dnmt3b also exhibited nonoverlapping functions in development, with Dnmt3b specifically required for methylation of centromeric minor satellite repeats. These results indicated that both Dnmt3a and Dnmt3b are required for genomewide de novo methylation and are essential for mammalian development.

[15784] It is appreciated that the abovementioned animal model for DNMT3B is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15785] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15786] Ehrlich, M.; Buchanan, K. L.; Tsien, F.; Jiang, G.; Sun, B.; Uicker, W.; Weemaes, C. M. R.; Smeets, D.; Sperling, K.; Belohradsky, B. H.; Tommerup, N.; Misek, D. E.; Rouillard, J.-M.; Kuick, R.; Hanash, S. M. : DNA methyltransferase 3B mutations linked to the ICF syndrome cause dysregulation of lymphogenesis genes. Hum. Molec. Genet. 10: 2917–2931, 2001. ; and

[15787] Rhee, I.; Bachman, K. E.; Park, B. H.; Jair, K.-W.; Yen, R.-W. C.; Schuebel, K. E.; Cui, H.; Feinberg, A. P.; Lengauer, C.; Kinzler, K. W.; Baylin, S. B.; Vogelstein, B. : DNMT1 and DNM.

[15788] Further studies establishing the function and utilities of DNMT3B are found in John Hopkins OMIM database record ID 602900, and in cited publications numbered 5910, 5781-5782, 11685, 6216, 1168 and 11686 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Mitogen-activated Protein Kinase Kinase 8 (MAP3K8, Accession NM_005204) is another VGAM280 host target gene. MAP3K8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MAP3K8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP3K8 BINDING SITE, designated SEQ ID:11705, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15789] Another function of VGAM280 is therefore inhibition of Mitogen-activated Protein Kinase Kinase Kinase 8 (MAP3K8, Accession NM_005204), a gene which is able to

activate nf-kappa-b 1 by stimulating proteasome-mediated p. Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP3K8. The function of MAP3K8 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM32.poly(A) Binding Protein, Cytoplasmic 1 (PABPC1, Accession NM_002568) is another VGAM280 host target gene. PABPC1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PABPC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PABPC1 BINDING SITE, designated SEQ ID:8420, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15790] Another function of VGAM280 is therefore inhibition of poly(A) Binding Protein, Cytoplasmic 1 (PABPC1, Accession NM_002568), a gene which involves in cytoplasmic regulatory processes of mRNA metabolism. Accordingly, utilities of VGAM280 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with PABPC1. The function of PABPC1 has been established by previous studies. The poly(A)-binding protein (PABP), which is found complexed to the 3-prime poly(A) tail of eukaryotic mRNA, is required for poly(A) shortening and translation initiation. Grange et al. (1987) isolated a melanoma cell cDNA encoding human PABP. The predicted 633-amino acid protein contains 4 repeats of an approximately 80-amino acid unit in its N-terminal half. The authors found that this repeat region is highly conserved between human and yeast PABP and is sufficient for poly(A) binding. In vitro translation of the human PABP cDNA yielded a protein with an apparent molecular mass of 73 kD by SDS-PAGE. Northern blot analysis indicated that PABP is expressed as a 2.9-kb mRNA in human melanoma cells. Gorlach et al. (1994) noted that each of the 4 repeats of PABP is a ribonucleoprotein (RNP) consensus sequence RNA-binding domain. They determined that PABP has a pI of approximately 10.3 and is a very abundant, stable protein. Immunofluorescence studies of mammalian cells indicated that PABP is located exclusively in the cytoplasm. However, using both indirect immunofluorescence and tagging of PABP1 by fusion to the

green fluorescent protein (GFP), Afonina et al. (1998) demonstrated that PABP1 shuttles between the nucleus and cytoplasm. PABP1 accumulated in the nucleus when transcription was inhibited, suggesting that active transcription is required for nuclear export of PABP1. Deletion mutagenesis showed that the RNA binding ability of PABP1 is important for nuclear retention. Afonina et al. (1998) suggested that PABP1 is involved in nuclear events associated with the formation and transport of mRNP to the cytoplasm. Deo et al. (1999) determined the cocrystal structure of human PABP at 2.6-angstrom resolution. PABP recognizes the 3-prime mRNA poly(A) tail and plays critical roles in eukaryotic translation initiation and mRNA stabilization/degradation. The minimal PABP used by Deo et al. (1999) consisted of the N-terminal 2 RRM-type RNA-binding domains connected by a short linker (collectively referred to as RRM1/2). These 2 RRMs form a continuous RNA-binding trough lined by an antiparallel beta sheet backed by 4 alpha helices. The polyadenylate RNA adopts an extended conformation running the length of the molecular trough. Adenine recognition is primarily mediated by contacts with conserved residues found in the RNP motifs of the 2 RRMs. The convex dorsum of

RRM1/2 displays a phylogenetically conserved hydrophobic/acidic portion, which may interact with translation initiation factors and regulatory proteins

[15791] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15792] Gorlach, M.; Burd, C. G.; Dreyfuss, G. : The mRNA poly(A)-binding protein: localization, abundance, and RNA-binding specificity. *Exp. Cell Res.* 211: 400-407, 1994. ; and

[15793] Deo, R. C.; Bonanno, J. B.; Sonenberg, N.; Burley, S. K. : Recognition of polyadenylate RNA by the poly(A)-binding protein. *Cell* 98: 835-845, 1999.

[15794] Further studies establishing the function and utilities of PABPC1 are found in John Hopkins OMIM database record ID 604679, and in cited publications numbered 7941-7942, 5300, 7943-794 and 11608 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 8 (sodium-calcium exchanger), Member 2 (SLC8A2, Accession XM_038970) is another VGAM280 host target gene. SLC8A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

SLC8A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC8A2 BINDING SITE, designated SEQ ID:32970, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15795] Another function of VGAM280 is therefore inhibition of Solute Carrier Family 8 (sodium–calcium exchanger), Member 2 (SLC8A2, Accession XM_038970). Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC8A2. FLJ13855 (Accession NM_023079) is another VGAM280 host target gene. FLJ13855 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ13855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13855 BINDING SITE, designated SEQ ID:23343, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15796] Another function of VGAM280 is therefore inhibition of

FLJ13855 (Accession NM_023079). Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13855. FLJ14431 (Accession NM_032783) is another VGAM280 host target gene. FLJ14431 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14431, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14431 BINDING SITE, designated SEQ ID:26528, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15797] Another function of VGAM280 is therefore inhibition of FLJ14431 (Accession NM_032783). Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14431. KIAA0373 (Accession NM_014684) is another VGAM280 host target gene. KIAA0373 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0373, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of KIAA0373 BINDING SITE, designated SEQ ID:16184, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15798] Another function of VGAM280 is therefore inhibition of KIAA0373 (Accession NM_014684). Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0373. Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM_005930) is another VGAM280 host target gene. MGEA6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGEA6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGEA6 BINDING SITE, designated SEQ ID:12560, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15799] Another function of VGAM280 is therefore inhibition of Meningioma Expressed Antigen 6 (coiled-coil proline-rich) (MGEA6, Accession NM_005930). Accordingly, utilities of VGAM280 include diagnosis, prevention and treat-

ment of diseases and clinical conditions associated with MGEA6. LOC116349 (Accession XM_057993) is another VGAM280 host target gene. LOC116349 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116349, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116349 BINDING SITE, designated SEQ ID:36556, to the nucleotide sequence of VGAM280 RNA, herein designated VGAM RNA, also designated SEQ ID:2991.

[15800] Another function of VGAM280 is therefore inhibition of LOC116349 (Accession XM_057993). Accordingly, utilities of VGAM280 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116349. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 281 (VGAM281) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15801] VGAM281 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM281 was detected is described hereinabove with reference to Figs. 1–8.

[15802] VGAM281 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15803] VGAM281 gene encodes a VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM281 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM281 precursor RNA is designated SEQ ID:267, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:267 is located at position 83939 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15804] VGAM281 precursor RNA folds onto itself, forming VGAM281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15805] An enzyme complex designated DICER COMPLEX, `dices` the VGAM281 folded precursor RNA into VGAM281 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM281 RNA is designated SEQ ID:2992, and is provided hereinbelow with reference to the sequence listing part.

[15806] VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM281 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15807] VGAM281 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM281 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM281 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15808] The complementary binding of VGAM281 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM281 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM281 host target RNA into VGAM281 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15809] It is appreciated that VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM281 host target genes. The mRNA of each one of this plurality of VGAM281 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM281 RNA, herein designated VGAM RNA, and which when bound by VGAM281 RNA causes inhibition of translation of respective one or more VGAM281 host target proteins.

[15810] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM281 gene, herein designated VGAM GENE, on one or more VGAM281 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15811] It is yet further appreciated that a function of VGAM281 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM281 correlate with, and may be deduced from, the identity of the host target genes which VGAM281 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15812] Nucleotide sequences of the VGAM281 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

5' duced 5' VGAM281 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM281 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM281 are further described hereinbelow with reference to Table 1.

[15813] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM281 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM281 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15814] As mentioned hereinabove with reference to Fig. 1, a function of VGAM281 gene, herein designated VGAM is inhibition of expression of VGAM281 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM281 correlate with, and may be deduced from, the identity of the target genes which VGAM281 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15815] CD28 Antigen (Tp44) (CD28, Accession NM_006139) is a VGAM281 host target gene. CD28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by CD28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD28 BINDING SITE, designated SEQ ID:12786, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15816] A function of VGAM281 is therefore inhibition of CD28 Antigen (Tp44) (CD28, Accession NM_006139), a gene which possibly involved in t-cell activation. Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD28. The function of CD28 has been established by previous studies. Monoclonal antibodies recognize 3 antigens, CD3 (OMIM Ref. No. 186790), CD2 (OMIM Ref. No. 186990), and CD28 (Tp44), that cause human T cells to proliferate in the presence of phorbol esters. Whereas CD3 appeared to be involved in transduction of the signal generated by antigen binding to the T-cell receptor, the role of the CD2 and CD28 antigens in physiologic proliferation was not understood. Aruffo and Seed (1987) isolated a cDNA clone encoding CD28 by a simple and highly efficient cloning strategy based on transient expression.

In COS cells the CD28 encodes a highly glycosylated membrane protein with homology to the immunoglobulin superfamily. Animal model experiments lend further support to the function of CD28. CD28 undergoes tyrosine phosphorylation after interacting with its ligand, B7 (CD80; 112203). Phosphorylation of tyr173 (tyr170 in mouse) in the cytoplasmic domain of CD28 allows the recruitment of signaling proteins such as phosphatidylinositol 3-kinase (see OMIM Ref. No. PIK3R1; 171833), GRB2 (OMIM Ref. No. 108355), and GADS (GRAP2; 604518) via their SH2 domains. Okkenhaug et al. (2001) reconstituted CD28 knockout mice with transgenes encoding wildtype Cd28 or Cd28 carrying a tyr170-to-phe mutation. Mutant Cd28 did not bind to the SH2 domain of PIK3R1, resulting in diminished protein kinase B (OMIM Ref. No. 164730) activation. Mutant Cd28 was able to prevent the induction of anergy, to promote T-cell proliferation and interleukin-2 (IL2; 147680) secretion, and to provide B-cell help, but was unable to upregulate expression of the prosurvival protein BCLXL (OMIM Ref. No. 600039). The defect in BCLXL upregulation was correlated with increased susceptibility of the T cells to gamma radiation. Okkenhaug et al. (2001) suggested that other tyrosine residues or asn172

may be critical to functions not affected by the tyr170-to-phe mutation.

[15817] It is appreciated that the abovementioned animal model for CD28 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15818] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15819] Aruffo, A.; Seed, B. : Molecular cloning of a CD28 cDNA by a high-efficiency COS cell expression system. Proc. Nat. Acad. Sci. 84: 8573-8577, 1987. ; and

[15820] Okkenhaug, K.; Wu, L.; Garza, K. M.; La Rose, J.; Khoo, W.; Odermatt, B.; Mak, T. W.; Ohashi, P. S.; Rottapel, R. : A point mutation in CD28 distinguishes proliferative signals from sur.

[15821] Further studies establishing the function and utilities of CD28 are found in John Hopkins OMIM database record ID 186760, and in cited publications numbered 5673-435 and 5674-5677 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Insulin Receptor Substrate 1 (IRS1, Accession NM_005544) is another VGAM281 host target gene. IRS1

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IRS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IRS1 BINDING SITE, designated SEQ ID:12069, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15822] Another function of VGAM281 is therefore inhibition of Insulin Receptor Substrate 1 (IRS1, Accession NM_005544), a gene which may mediate the control of various cellular processes by insulin. Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IRS1. The function of IRS1 has been established by previous studies. Sun et al. (1991) isolated cDNAs encoding a 160- to 185-kD phosphotyrosyl protein that is a substrate of the insulin receptor tyrosine kinase and a putative participant in insulin (INS; 176730) signaling. This protein, designated insulin receptor substrate-1 (IRS1), is found in a variety of insulin responsive cells and tissues. It exhibits no intrinsic enzyme activity but is believed to serve as a docking protein involved in binding and activating other

signal transduction molecules after being phosphorylated on tyrosine by the insulin receptor kinase Almind et al. (1996) examined insulin-stimulated processes in a cultured myeloid progenitor cell stably overexpressing the insulin receptor when transfected with either wildtype human IRS1 or the gly972-to-arg common variant (numbering according to Nishiyama and Wands, 1992). They showed that the mutation in codon 972 of the IRS1 gene impairs insulin-stimulated signaling, especially along the phosphatidylinositol 3-kinase (OMIM Ref. No. 171834) pathway, and may contribute to insulin resistance in normal and diabetic populations. Animal model experiments lend further support to the function of IRS1. Clancy et al. (2001) found that mutation of chico extends fruit fly lifespan by up to 48% in homozygotes and 36% in heterozygotes. Extension of lifespan was not a result of impaired oogenesis in chico females, nor was it consistently correlated with increased stress resistance. The dwarf phenotype of chico homozygotes was also unnecessary for extension of lifespan. The role of insulin/IGF signaling in regulating animal aging is therefore evolutionarily conserved

[15823] It is appreciated that the abovementioned animal model

for IRS1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15824] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15825] Esposito, D. L.; Mammarella, S.; Ranieri, A.; Loggia, F. D.; Capani, F.; Consoli, A.; Mariani-Costantini, R.; Caramia, F. G.; Cama, A.; Battista, P. : Deletion of gly723 in the insulin receptor substrate-1 of a patient with noninsulin-dependent diabetes mellitus. Hum. Mutat. 7: 364-366, 1996. ; and

[15826] Almind, K.; Inoue, G.; Pedersen, O.; Kahn, C. R. : A common amino acid polymorphism in insulin receptor substrate-1 causes impaired insulin signaling: evidence from transfection studies.

[15827] Further studies establishing the function and utilities of IRS1 are found in John Hopkins OMIM database record ID 147545, and in cited publications numbered 129-135, 445 and 4459-4472 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269) is another VGAM281 host target gene.

LEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEF1 BINDING SITE, designated SEQ ID:18393, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15828] Another function of VGAM281 is therefore inhibition of Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269), a gene which plays an essential role in the formation of several organs and structures that require inductive tissue interactions. Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEF1. The function of LEF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Matrix Metalloproteinase 19 (MMP19, Accession NM_022790) is another VGAM281 host target gene. MMP19 BINDING SITE1 and MMP19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MMP19, corresponding to HOST

TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP19 BINDING SITE1 and MMP19 BINDING SITE2, designated SEQ ID:23078 and SEQ ID:8270 respectively, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15829] Another function of VGAM281 is therefore inhibition of Matrix Metalloproteinase 19 (MMP19, Accession NM_022790). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP19. Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063) is another VGAM281 host target gene. EML4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EML4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EML4 BINDING SITE, designated SEQ ID:21143, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15830] Another function of VGAM281 is therefore inhibition of

Echinoderm Microtubule Associated Protein Like 4 (EML4, Accession NM_019063). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EML4. FLJ22969 (Accession XM_044006) is another VGAM281 host target gene. FLJ22969 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22969, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22969 BINDING SITE, designated SEQ ID:34066, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15831] Another function of VGAM281 is therefore inhibition of FLJ22969 (Accession XM_044006). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22969. FLJ23153 (Accession NM_024636) is another VGAM281 host target gene. FLJ23153 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23153, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23153 BINDING SITE, designated SEQ ID:23906, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15832] Another function of VGAM281 is therefore inhibition of FLJ23153 (Accession NM_024636). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23153. FLJ30567 (Accession NM_145022) is another VGAM281 host target gene. FLJ30567 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30567, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30567 BINDING SITE, designated SEQ ID:29635, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15833] Another function of VGAM281 is therefore inhibition of FLJ30567 (Accession NM_145022). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30567.

KIAA1946 (Accession XM_092459) is another VGAM281 host target gene. KIAA1946 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1946, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1946 BINDING SITE, designated SEQ ID:40122, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15834] Another function of VGAM281 is therefore inhibition of KIAA1946 (Accession XM_092459). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1946. Phosphodiesterase 11A (PDE11A, Accession NM_016953) is another VGAM281 host target gene. PDE11A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PDE11A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PDE11A BINDING SITE, designated SEQ ID:18869, to the nucleotide sequence of VGAM281 RNA,

herein designated VGAM RNA, also designated SEQ ID:2992.

[15835] Another function of VGAM281 is therefore inhibition of Phosphodiesterase 11A (PDE11A, Accession NM_016953). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PDE11A. TUCAN (Accession NM_014959) is another VGAM281 host target gene. TUCAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUCAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUCAN BINDING SITE, designated SEQ ID:17320, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15836] Another function of VGAM281 is therefore inhibition of TUCAN (Accession NM_014959). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUCAN. LOC118851 (Accession XM_061180) is another VGAM281 host target gene. LOC118851 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of

mRNA encoded by LOC118851, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC118851 BINDING SITE, designated SEQ ID:37205, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15837] Another function of VGAM281 is therefore inhibition of LOC118851 (Accession XM_061180). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC118851. LOC144742 (Accession XM_084949) is another VGAM281 host target gene. LOC144742 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC144742, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144742 BINDING SITE, designated SEQ ID:37778, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15838] Another function of VGAM281 is therefore inhibition of LOC144742 (Accession XM_084949). Accordingly, utilities

of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144742. LOC147353 (Accession XM_097227) is another VGAM281 host target gene. LOC147353 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147353, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147353 BINDING SITE, designated SEQ ID:40838, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15839] Another function of VGAM281 is therefore inhibition of LOC147353 (Accession XM_097227). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147353. LOC221687 (Accession XM_166423) is another VGAM281 host target gene. LOC221687 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221687, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC221687 BINDING SITE, designated SEQ ID:44301, to the nucleotide sequence of VGAM281 RNA, herein designated VGAM RNA, also designated SEQ ID:2992.

[15840] Another function of VGAM281 is therefore inhibition of LOC221687 (Accession XM_166423). Accordingly, utilities of VGAM281 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221687. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 282 (VGAM282) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15841] VGAM282 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM282 was detected is described hereinabove with reference to Figs. 1–8.

[15842] VGAM282 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15843] VGAM282 gene encodes a VGAM282 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM282 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM282 precursor RNA is designated SEQ ID:268, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:268 is located at position 78903 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15844] VGAM282 precursor RNA folds onto itself, forming VGAM282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15845] An enzyme complex designated DICER COMPLEX, `dices` the VGAM282 folded precursor RNA into VGAM282 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM282 RNA is designated SEQ ID:2993, and is provided hereinbelow with reference to the sequence listing part.

[15846] VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM282 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15847] VGAM282 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM282 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM282 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15848] The complementary binding of VGAM282 RNA, herein designated VGAM RNA, to host target binding sites on VGAM282 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM282 host target RNA into VGAM282 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15849] It is appreciated that VGAM282 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM282 host target genes. The mRNA of each one of this plurality of VGAM282 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM282 RNA, herein designated VGAM RNA, and which when bound by VGAM282 RNA causes inhibition of translation of respective one or more VGAM282 host target proteins.

[15850] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM282 gene, herein designated VGAM GENE, on one or more VGAM282 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[15851] It is yet further appreciated that a function of VGAM282 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM282 correlate with, and may be deduced from, the identity of the host target genes which VGAM282 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15852] Nucleotide sequences of the VGAM282 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM282 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM282 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM282 are further described hereinbelow with reference to Table 1.

[15853] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM282 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM282 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15854] As mentioned hereinabove with reference to Fig. 1, a function of VGAM282 gene, herein designated VGAM is inhibition of expression of VGAM282 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM282 correlate with, and may be deduced from, the identity of the target genes which VGAM282 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15855] Arachidonate 15-lipoxygenase (ALOX15, Accession NM_001140) is a VGAM282 host target gene. ALOX15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALOX15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALOX15 BINDING SITE, designated SEQ ID:6810, to the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, also designated SEQ ID:2993.

[15856] A function of VGAM282 is therefore inhibition of Arachidonate 15-lipoxygenase (ALOX15, Accession NM_001140), a gene which converts arachidonic acid to 15s- hydroperoxyeicosatetraenoic acid. Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALOX15. The function of ALOX15 has been established by previous studies. Yoshimoto et al. (1990) found that the amino acid sequence of human reticulocyte 15-lipoxygenase (Sigal et al., 1988) showed 86% identity with that of porcine leukocyte 12-lipoxygenase (OMIM Ref. No. 152391). Sigal et al. (1988) found 61% sequence similarity between 15-lipoxygenase and 5-lipoxygenase (OMIM Ref. No. 152390). This suggests that in the human 12-lipoxygenase is more closely related evolutionarily to 15-lipoxygenase than to 5-lipoxygenase, even though the comparisons are made between human and porcine enzymes. By PCR analysis of a human-hamster somatic hybrid DNA panel, Funk et al. (1992) demonstrated that genes for 12-lipoxygenase and 15-lipoxygenase are located on human chromosome 17, whereas the most unrelated lipoxygenase (5-lipoxygenase) was mapped to chromosome 10. Kelavkar and Badr (1999) stated that the

ALOX15 gene maps to 17p13.3 in close proximity to the tumor-suppressor gene TP53 (OMIM Ref. No. 191170). The ALOX15 gene product is implicated in antiinflammation, membrane remodeling, and cancer development/metastasis. Kelavkar and Badr (1999) described experiments yielding data that supported the hypothesis that loss of the TP53 gene, or gain-of-function activities resulting from the expression of its mutant forms, regulates ALOX15 promoter activity in human and in mouse, albeit in directionally opposite manners. These studies defined a direct link between ALOX15 gene activity and an established tumor-suppressor gene located in close chromosomal proximity. Kelavkar and Badr (1999) referred to this as evidence that 15-lipoxygenase is a mutator gene.

[15857] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15858] Kelavkar, U. P.; Badr, K. F. : Effects of mutant p53 expression on human 15-lipoxygenase-promoter activity and murine 12/15-lipoxygenase gene expression: evidence that 15-lipoxygenase is a mutator gene. Proc. Nat. Acad. Sci. 96: 4378-4383, 1999. ; and

[15859] Yoshimoto, T.; Suzuki, H.; Yamamoto, S.; Takai, T.;

Yokoyama, C.; Tanabe, T. : Cloning and sequence analysis of the cDNA for arachidonate 12-lipoxygenase of porcine leukocytes. Proc. Na.

[15860] Further studies establishing the function and utilities of ALOX15 are found in John Hopkins OMIM database record ID 152392, and in cited publications numbered 169 and 3430–3432 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Deleted In Azoospermia (DAZ, Accession NM_004081) is another VGAM282 host target gene. DAZ BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by DAZ, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAZ BINDING SITE, designated SEQ ID:10281, to the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, also designated SEQ ID:2993.

[15861] Another function of VGAM282 is therefore inhibition of Deleted In Azoospermia (DAZ, Accession NM_004081), a gene which may play a role in the germ-cell-specific patterns of RNA splicing and storage. Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with DAZ. The function of DAZ and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM206.Solute Carrier Family 6 (neurotransmitter transporter, glycine), Member 5 (SLC6A5, Accession NM_004211) is another VGAM282 host target gene. SLC6A5 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLC6A5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A5 BINDING SITE, designated SEQ ID:10417, to the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, also designated SEQ ID:2993.

[15862] Another function of VGAM282 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, glycine), Member 5 (SLC6A5, Accession NM_004211), a gene which terminates the action of glycine by its high affinity sodium-dependent reuptake into presynaptic terminals. Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with SLC6A5. The function of SLC6A5 has been established by previous studies. The amino acid glycine is a major inhibitory neurotransmitter in the spinal cord, brainstem, and retina, where it exerts its effects on the strychnine-sensitive glycine receptors. In addition, glycine acts as a coagonist with glutamate at the N-methyl-D-aspartate (NMDA) receptors (see OMIM Ref. No. 138252). The termination of action of glycine, like that of most other neurotransmitters, is mediated by rapid reuptake into the presynaptic terminal or surrounding glial cells. Glycine transporters are members of the sodium/chloride-dependent transporter family, which share 40 to 50% amino acid similarity and are characterized by 12 putative transmembrane regions. Liu et al. (1993) isolated a rat brain cDNA encoding a novel glycine transporter, which they called GlyT2. They found that GlyT2 differs from GlyT1 (OMIM Ref. No. 601019) in molecular structure, tissue specificity, and pharmacologic properties. By PCR of a human brain cDNA library with primers based on conserved regions of the rat GlyT2 gene, Morrow et al. (1998) cloned a cDNA corresponding to human GLYT2. The predicted 797-amino acid human protein is 94% identical to rat GlyT2. When expressed in mammalian

cells, GLYT2 displayed high affinity glycine uptake. Northern blot analysis of central nervous system tissues revealed that the approximately 9.5-kb GLYT2 mRNA is expressed in medulla, and to a lesser extent in spinal cord and cerebellum. Morrow et al. (1998) stated that the previously characterized GLYT1 and GLYT2 localization patterns suggest that GLYT2 is responsible for the termination of neurotransmission at strychnine-sensitive glycinergic synapses, while the more widely expressed GLYT1 may play a role in regulation of glycine levels in NMDA receptor-mediated neurotransmission. Independently, Gallagher et al. (1999) isolated cDNAs encoding 3 isoforms of GLYT2

[15863] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15864] Liu, Q. R.; Lopez-Corcuera, B.; Mandiyan, S.; Nelson, H.; Nelson, N. : Cloning and expression of a spinal cord- and brain-specific glycine transporter with novel structural features. J. Biol. Chem. 268: 22802-22808, 1993. ; and

[15865] Morrow, J. A.; Collie, I. T.; Dunbar, D. R.; Walker, G. B.; Shahid, M.; Hill, D. R. : Molecular cloning and functional expression of the human glycine transporter GlyT2 and

chromosomal I.

[15866] Further studies establishing the function and utilities of SLC6A5 are found in John Hopkins OMIM database record ID 604159, and in cited publications numbered 427–42 and 7938 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332) is another VGAM282 host target gene. WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WHSC1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WHSC1 BINDING SITE1 through WHSC1 BINDING SITE3, designated SEQ ID:28450, SEQ ID:28467 and SEQ ID:17186 respectively, to the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, also designated SEQ ID:2993.

[15867] Another function of VGAM282 is therefore inhibition of Wolf–Hirschhorn Syndrome Candidate 1 (WHSC1, Accession NM_133332), a gene which binds covalently to and repairs g/t mismatches. Accordingly, utilities of VGAM282

include diagnosis, prevention and treatment of diseases and clinical conditions associated with WHSC1. The function of WHSC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. LOC150280 (Accession XM_086846) is another VGAM282 host target gene. LOC150280 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150280 BINDING SITE, designated SEQ ID:38912, to the nucleotide sequence of VGAM282 RNA, herein designated VGAM RNA, also designated SEQ ID:2993.

[15868] Another function of VGAM282 is therefore inhibition of LOC150280 (Accession XM_086846). Accordingly, utilities of VGAM282 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150280. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 283 (VGAM283) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15869] VGAM283 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM283 was detected is described hereinabove with reference to Figs. 1–8.

[15870] VGAM283 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15871] VGAM283 gene encodes a VGAM283 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM283 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM283 precursor RNA is designated SEQ ID:269, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:269 is located at position 1023 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15872] VGAM283 precursor RNA folds onto itself, forming

VGAM283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15873] An enzyme complex designated DICER COMPLEX, `dices` the VGAM283 folded precursor RNA into VGAM283 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM283 RNA is designated SEQ ID:2994, and is provided hereinbelow with reference to the sequence listing part.

[15874] VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM283 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15875] VGAM283 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM283 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM283 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15876] The complementary binding of VGAM283 RNA, herein designated VGAM RNA, to host target binding sites on VGAM283 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM283 host target RNA into VGAM283 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15877] It is appreciated that VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM283 host target genes. The mRNA of each one of this plurality of VGAM283 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM283 RNA, herein designated VGAM RNA, and which when bound by VGAM283 RNA causes inhibition of translation of respective one or more VGAM283 host target proteins.

[15878] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM283 gene, herein designated VGAM GENE, on one or more VGAM283 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15879] It is yet further appreciated that a function of VGAM283 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM283 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM283 correlate with, and may be deduced from, the identity of the host target genes which

VGAM283 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15880] Nucleotide sequences of the VGAM283 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM283 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM283 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM283 are further described hereinbelow with reference to Table 1.

[15881] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM283 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM283 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15882] As mentioned hereinabove with reference to Fig. 1, a function of VGAM283 gene, herein designated VGAM is inhibition of expression of VGAM283 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM283 correlate with, and may be deduced from, the identity of the target genes which VGAM283 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[15883] Dual Adaptor of Phosphotyrosine and 3-phosphoinositides (DAPP1, Accession NM_014395) is a VGAM283 host target gene. DAPP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAPP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAPP1 BINDING SITE, designated SEQ ID:15731, to the nucleotide sequence of VGAM283 RNA, herein designated VGAM RNA, also designated SEQ ID:2994.

[15884] A function of VGAM283 is therefore inhibition of Dual Adaptor of Phosphotyrosine and 3-phosphoinositides (DAPP1, Accession NM_014395), a gene which regulates the ras-cyclic amp pathway. Accordingly, utilities of VGAM283 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DAPP1. The function of DAPP1 has been established by previous studies. By EST database searching for pleckstrin homology (PH) domain-containing proteins, followed by screening a universal cDNA library, Dowler et al. (1999) isolated a cDNA encoding DAPP1. Sequence analysis predicted that

the 280-amino acid protein contains a potential myristoylation site (a glycine after the N-terminal methionine), an N-terminal SH2 domain, and a C-terminal PH domain with a PtdIns-interacting motif. The authors noted that APS (OMIM Ref. No. 605300) also has an SH2 domain and a PH domain but at opposite termini of the protein. PCR of cDNA libraries and Northern blot analysis revealed ubiquitous expression of 2.7-kb transcripts, with highest levels in placenta and lung. A protein-lipid overlay analysis indicated that the PH domain of DAPP1 interacts with physiologic enantiomers of PtdIns. Using suppression subtractive hybridization with follicular dendritic cell tester cDNA, Marshall et al. (2000) cloned BAM32 and a splice variant identical to DAPP1. In addition to the SH2 and PH domains noted by Dowler et al. (1999), Marshall et al. (2000) predicted the presence of a potential tyrosine phosphorylation site in BAM32. Northern blot analysis detected an abundant 2.9-kb transcript and a minor 4.4-kb transcript in all hemopoietic tissues, as well as in trachea and placenta. RT-PCR analysis revealed expression in all B-cell lines, but not in T-cell, epithelial cell, fibroblast, or myelocytic leukemia cell lines. Activation of B cells was found to increase BAM32 expression. Immunoblot analysis

showed that stimulation also induces BAM32 association with PLCG2 (OMIM Ref. No. 600220) and tyrosine phosphorylation of a 36-kD protein. Confocal microscopy demonstrated a PI3K-dependent membrane localization of BAM32 after B-cell receptor (BCR) activation. Luciferase reporter analysis showed that expression of the PH domain of BAM32 inhibits BCR-induced activation of NFATC (see OMIM Ref. No. 600489).

[15885] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15886] Dowler, S.; Currie, R. A.; Downes, C. P.; Alessi, D. R. : DAPP1: a dual adaptor for phosphotyrosine and 3-phosphoinositides. *Biochem. J.* 342: 7-12, 1999. ; and

[15887] Marshall, A. J.; Niiro, H.; Lerner, C. G.; Yun, T. J.; Thomas, S.; Disteche, C. M.; Clark, E. A. : A novel B lymphocyte-associated adaptor protein, Bam32, regulates antigen receptor si.

[15888] Further studies establishing the function and utilities of DAPP1 are found in John Hopkins OMIM database record ID 605768, and in cited publications numbered 4506-4507 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Fig. 1

further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 284 (VGAM284) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15889] VGAM284 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM284 was detected is described hereinabove with reference to Figs. 1–8.

[15890] VGAM284 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15891] VGAM284 gene encodes a VGAM284 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM284 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM284 precursor RNA is designated SEQ ID:270, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:270 is

located at position 5957 relative to the genome of Epi-
phyas Postvittana Nucleopolyhedrovirus.

[15892] VGAM284 precursor RNA folds onto itself, forming VGAM284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15893] An enzyme complex designated DICER COMPLEX, `dices` the VGAM284 folded precursor RNA into VGAM284 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM284 RNA is designated SEQ ID:2995, and is provided hereinbelow with reference to the sequence listing part.

[15894] VGAM284 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM284 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[15895] VGAM284 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM284 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM284 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM284 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[15896] The complementary binding of VGAM284 RNA, herein designated VGAM RNA, to host target binding sites on VGAM284 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM284 host target RNA into VGAM284 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15897] It is appreciated that VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM284 host target genes. The mRNA of each one of this plurality of VGAM284 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM284 RNA, herein designated VGAM RNA, and which when bound by VGAM284 RNA causes inhibition of translation of respective one or more VGAM284

host target proteins.

[15898] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM284 gene, herein designated VGAM GENE, on one or more VGAM284 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15899] It is yet further appreciated that a function of VGAM284 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM284 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucle-

opolyhedrovirus. Specific functions, and accordingly utilities, of VGAM284 correlate with, and may be deduced from, the identity of the host target genes which VGAM284 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15900] Nucleotide sequences of the VGAM284 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM284 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM284 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM284 are further described hereinbelow with reference to Table 1.

[15901] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM284 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM284 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15902] As mentioned hereinabove with reference to Fig. 1, a function of VGAM284 gene, herein designated VGAM is inhibition of expression of VGAM284 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM284 correlate with, and may be deduced from, the identity of the target genes which VGAM284 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15903] MGC12538 (Accession NM_032746) is a VGAM284 host target gene. MGC12538 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC12538, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC12538 BINDING SITE, designated SEQ ID:26479, to the nucleotide sequence of VGAM284 RNA, herein designated VGAM RNA, also designated SEQ ID:2995.

[15904] A function of VGAM284 is therefore inhibition of MGC12538 (Accession NM_032746). Accordingly, utilities of VGAM284 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC12538. Nucleoporin 160kDa (NUP160, Accession XM_113678) is another VGAM284 host target gene. NUP160 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NUP160, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NUP160 BINDING SITE, designated SEQ ID:42327, to the nucleotide sequence of VGAM284 RNA, herein designated VGAM RNA, also designated SEQ ID:2995.

[15905] Another function of VGAM284 is therefore inhibition of Nucleoporin 160kDa (NUP160, Accession XM_113678). Accordingly, utilities of VGAM284 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NUP160. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 285 (VGAM285) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15906] VGAM285 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM285 was detected is described hereinabove with reference to Figs. 1–8.

[15907] VGAM285 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana

Nucleopolyhedrovirus. VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15908] VGAM285 gene encodes a VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM285 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM285 precursor RNA is designated SEQ ID:271, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:271 is located at position 58647 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[15909] VGAM285 precursor RNA folds onto itself, forming VGAM285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15910] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM285 folded precursor RNA into VGAM285 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM285 RNA is designated SEQ ID:2996, and is provided hereinbelow with reference to the sequence listing part.

[15911] VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM285 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15912] VGAM285 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM285 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM285 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15913] The complementary binding of VGAM285 RNA, herein designated VGAM RNA, to host target binding sites on VGAM285 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM285 host target RNA into VGAM285 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15914] It is appreciated that VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM285 host target genes. The mRNA of each one of this plurality of VGAM285 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM285 RNA, herein designated VGAM RNA, and which when bound by VGAM285 RNA causes inhibition of translation of respective one or more VGAM285 host target proteins.

[15915] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM285 gene, herein designated VGAM GENE, on one or more VGAM285 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15916] It is yet further appreciated that a function of VGAM285 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM285 correlate with, and may be deduced from, the identity of the host target genes which VGAM285 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15917] Nucleotide sequences of the VGAM285 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM285 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM285 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM285 are further described hereinbelow with reference to Table 1.

[15918] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM285 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM285 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15919] As mentioned hereinabove with reference to Fig. 1, a function of VGAM285 gene, herein designated VGAM is inhibition of expression of VGAM285 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM285 correlate with, and may be deduced from, the identity of the target genes which VGAM285 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15920] NEBL (Accession NM_006393) is a VGAM285 host target gene. NEBL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEBL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEBL BINDING SITE, designated SEQ ID:13100, to the nucleotide sequence of VGAM285 RNA, herein des-

ignated VGAM RNA, also designated SEQ ID:2996.

[15921] A function of VGAM285 is therefore inhibition of NEBL (Accession NM_006393). Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEBL. FLJ12389 (Accession XM_015274) is another VGAM285 host target gene. FLJ12389 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12389, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12389 BINDING SITE, designated SEQ ID:30235, to the nucleotide sequence of VGAM285 RNA, herein designated VGAM RNA, also designated SEQ ID:2996.

[15922] Another function of VGAM285 is therefore inhibition of FLJ12389 (Accession XM_015274). Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12389. FLJ20300 (Accession NM_017753) is another VGAM285 host target gene. FLJ20300 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20300, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20300 BINDING SITE, designated SEQ ID:19366, to the nucleotide sequence of VGAM285 RNA, herein designated VGAM RNA, also designated SEQ ID:2996.

[15923] Another function of VGAM285 is therefore inhibition of FLJ20300 (Accession NM_017753). Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20300. LOC147054 (Accession XM_097172) is another VGAM285 host target gene. LOC147054 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147054, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147054 BINDING SITE, designated SEQ ID:40795, to the nucleotide sequence of VGAM285 RNA, herein designated VGAM RNA, also designated SEQ ID:2996.

[15924] Another function of VGAM285 is therefore inhibition of LOC147054 (Accession XM_097172). Accordingly, utilities of VGAM285 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC147054. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 286 (VGAM286) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15925] VGAM286 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM286 was detected is described hereinabove with reference to Figs. 1–8.

[15926] VGAM286 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15927] VGAM286 gene encodes a VGAM286 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM286 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM286 precursor RNA is designated SEQ

ID:272, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:272 is located at position 4528 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15928] VGAM286 precursor RNA folds onto itself, forming VGAM286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15929] An enzyme complex designated DICER COMPLEX, `dices` the VGAM286 folded precursor RNA into VGAM286 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM286 RNA is designated SEQ ID:2997, and is provided hereinbelow with reference to the sequence

listing part.

[15930] VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM286 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15931] VGAM286 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM286 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM286 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15932] The complementary binding of VGAM286 RNA, herein designated VGAM RNA, to host target binding sites on VGAM286 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM286 host target RNA into VGAM286 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15933] It is appreciated that VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM286 host target genes. The mRNA of each one of this plurality of VGAM286 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM286 RNA, herein designated VGAM

RNA, and which when bound by VGAM286 RNA causes inhibition of translation of respective one or more VGAM286 host target proteins.

[15934] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM286 gene, herein designated VGAM GENE, on one or more VGAM286 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15935] It is yet further appreciated that a function of VGAM286 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM286 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM286 correlate with, and may be deduced from, the identity of the host target genes which VGAM286 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15936] Nucleotide sequences of the VGAM286 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM286 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM286 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM286 are further described hereinbelow with reference to Table 1.

[15937] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM286 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM286 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15938] As mentioned hereinabove with reference to Fig. 1, a function of VGAM286 gene, herein designated VGAM is

inhibition of expression of VGAM286 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM286 correlate with, and may be deduced from, the identity of the target genes which VGAM286 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15939] Carcinoembryonic Antigen-related Cell Adhesion Molecule 6 (non-specific cross reacting antigen) (CEACAM6, Accession NM_002483) is a VGAM286 host target gene. CEACAM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CEACAM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEACAM6 BINDING SITE, designated SEQ ID:8308, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15940] A function of VGAM286 is therefore inhibition of Carcinoembryonic Antigen-related Cell Adhesion Molecule 6 (non-specific cross reacting antigen) (CEACAM6, Accession NM_002483), a gene which Non-specific cross reacting antigen (. Accordingly, utilities of VGAM286 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with CEACAM6. The function of CEACAM6 has been established by previous studies. Carcinoembryonic antigen (CEA; 114890) is one of the most widely used tumor markers in serum immunoassay determinations of carcinoma. An apparent lack of absolute cancer specificity for CEA probably results in part from the presence in normal and neoplastic tissues of antigens that share antigenic determinants with the 180-kD form of CEA. Barnett et al. (1988) presented sequences of a 'normal crossreacting antigen' (NCA) and showed that CEA and NCA, although closely related in sequence, are structurally and probably functionally distinct. Nomenclature: Beauchemin et al. (1999) provided a revised nomenclature for the CEA gene family. Based on this nomenclature, the CEA family is composed of the PSG subfamily (see OMIM Ref. No. 176392); the CEACAM subfamily, which includes CEACAM1 (BGP), CEACAM3 (CGM1), CEACAM4 (CGM7), CEACAM5 (CEA), CEACAM6 (NCA), CEACAM7 (CGM2), and CEACAM8 (CGM6); and the CEACAM pseudogene (CEACAMP) subfamily, CEACAMP1 through CEACAMP11, which had originally been named CGM8 through CGM18 (see OMIM Ref. No. 109770). The NCA gene was renamed

CEACAM6.

- [15941] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [15942] Barnett, T.; Goebel, S. J.; Nothdurft, M. A.; Elting, J. J. : Carcinoembryonic antigen family: characterization of cDNAs coding for NCA and CEA and suggestion of nonrandom sequence variation in their conserved loop-domains. *Genomics* 3: 59–66, 1988. ; and
- [15943] Beauchemin, N.; Draber, P.; Dveksler, G.; Gold, P.; Gray-Owen, S.; Grunert, F.; Hammarstrom, S.; Holmes, K. V.; Karlsson, A.; Kuroki, M.; Lin, S.-H.; Lucka, L.; and 13 others : Redefined.
- [15944] Further studies establishing the function and utilities of CEACAM6 are found in John Hopkins OMIM database record ID 163980, and in cited publications numbered 4 and 2240–2242 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Coagulation Factor C Homolog, Cochlin (*Limulus polyphemus*) (COCH, Accession NM_004086) is another VGAM286 host target gene. COCH BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COCH, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COCH BINDING SITE, designated SEQ ID:10291, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15945] Another function of VGAM286 is therefore inhibition of Coagulation Factor C Homolog, Cochlin (*Limulus polyphemus*) (COCH, Accession NM_004086). Accordingly, utilities of VGAM286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COCH. JJAZ1 (Accession NM_015355) is another VGAM286 host target gene. JJAZ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JJAZ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JJAZ1 BINDING SITE, designated SEQ ID:17653, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15946] Another function of VGAM286 is therefore inhibition of JJAZ1 (Accession NM_015355), a gene which is a zinc fin-

ger protein. Accordingly, utilities of VGAM286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JJAZ1. The function of JJAZ1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to

VGAM231.KIAA1223 (Accession XM_048747) is another VGAM286 host target gene. KIAA1223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1223 BINDING SITE, designated SEQ ID:35243, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15947] Another function of VGAM286 is therefore inhibition of KIAA1223 (Accession XM_048747). Accordingly, utilities of VGAM286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. MGC4655 (Accession NM_033309) is another VGAM286 host target gene. MGC4655 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MGC4655, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4655 BINDING SITE, designated SEQ ID:27144, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15948] Another function of VGAM286 is therefore inhibition of MGC4655 (Accession NM_033309). Accordingly, utilities of VGAM286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4655. R32184_3 (Accession NM_033420) is another VGAM286 host target gene. R32184_3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by R32184_3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of R32184_3 BINDING SITE, designated SEQ ID:27247, to the nucleotide sequence of VGAM286 RNA, herein designated VGAM RNA, also designated SEQ ID:2997.

[15949] Another function of VGAM286 is therefore inhibition of R32184_3 (Accession NM_033420). Accordingly, utilities

of VGAM286 include diagnosis, prevention and treatment of diseases and clinical conditions associated with R32184_3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 287 (VGAM287) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15950] VGAM287 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM287 was detected is described hereinabove with reference to Figs. 1–8.

[15951] VGAM287 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15952] VGAM287 gene encodes a VGAM287 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM287 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM287 precursor RNA is designated SEQ ID:273, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:273 is located at position 89234 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15953] VGAM287 precursor RNA folds onto itself, forming VGAM287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15954] An enzyme complex designated DICER COMPLEX, `dices` the VGAM287 folded precursor RNA into VGAM287 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM287 RNA is designated SEQ ID:2998, and

is provided hereinbelow with reference to the sequence listing part.

[15955] VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM287 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15956] VGAM287 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM287 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM287 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[15957] The complementary binding of VGAM287 RNA, herein designated VGAM RNA, to host target binding sites on VGAM287 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM287 host target RNA into VGAM287 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15958] It is appreciated that VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM287 host target genes. The mRNA of each one of this plurality of VGAM287 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM287 RNA, herein designated VGAM RNA, and which when bound by VGAM287 RNA causes inhibition of translation of respective one or more VGAM287 host target proteins.

[15959] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM287 gene, herein designated VGAM GENE, on one or more VGAM287 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15960] It is yet further appreciated that a function of VGAM287 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM287 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM287 correlate with, and may be deduced from, the identity of the host target genes which VGAM287 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15961] Nucleotide sequences of the VGAM287 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM287 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM287 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM287 are further described hereinbelow with reference to Table 1.

[15962] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM287 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM287 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15963] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM287 gene, herein designated VGAM is inhibition of expression of VGAM287 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM287 correlate with, and may be deduced from, the identity of the target genes which VGAM287 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15964] Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen debranching enzyme, glycogen storage disease type III) (AGL, Accession NM_000028) is a VGAM287 host target gene. AGL BINDING SITE1 through AGL BINDING SITE6 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by AGL, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AGL BINDING SITE1 through AGL BINDING SITE6, designated SEQ ID:5467, SEQ ID:6284, SEQ ID:6289, SEQ ID:6294, SEQ ID:6299 and SEQ ID:6306 respectively, to the nucleotide sequence of VGAM287 RNA, herein designated VGAM RNA, also designated SEQ ID:2998.

[15965] A function of VGAM287 is therefore inhibition of Amylo-1, 6-glucosidase, 4-alpha-glucanotransferase (glycogen de-

branching enzyme, glycogen storage disease type III) (AGL, Accession NM_000028). Accordingly, utilities of VGAM287 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AGL. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 288 (VGAM288) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[15966] VGAM288 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM288 was detected is described hereinabove with reference to Figs. 1–8.

[15967] VGAM288 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[15968] VGAM288 gene encodes a VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM288 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM288 precursor RNA is designated SEQ ID:274, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:274 is located at position 54105 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[15969] VGAM288 precursor RNA folds onto itself, forming VGAM288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[15970] An enzyme complex designated DICER COMPLEX, `dices` the VGAM288 folded precursor RNA into VGAM288 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide se-

quence of VGAM288 RNA is designated SEQ ID:2999, and is provided hereinbelow with reference to the sequence listing part.

[15971] VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM288 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[15972] VGAM288 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM288 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM288 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[15973] The complementary binding of VGAM288 RNA, herein designated VGAM RNA, to host target binding sites on VGAM288 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM288 host target RNA into VGAM288 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[15974] It is appreciated that VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM288 host target genes. The mRNA of each one of this plurality of VGAM288 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM288 RNA, herein designated VGAM RNA, and which when bound by VGAM288 RNA causes inhibition of translation of respective one or more VGAM288 host target proteins.

[15975] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM288 gene, herein designated VGAM GENE, on one or more VGAM288 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[15976] It is yet further appreciated that a function of VGAM288 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM288 correlate with, and may be deduced from, the identity of the host target genes which VGAM288 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[15977] Nucleotide sequences of the VGAM288 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM288 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM288 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM288 are further described hereinbelow with reference to Table 1.

[15978] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM288 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM288 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[15979] As mentioned hereinabove with reference to Fig. 1, a function of VGAM288 gene, herein designated VGAM is inhibition of expression of VGAM288 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM288 correlate with, and may be deduced from, the identity of the target genes which VGAM288 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[15980] IL2-inducible T-cell Kinase (ITK, Accession NM_005546) is a VGAM288 host target gene. ITK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITK BINDING SITE, designated SEQ ID:12076, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15981] A function of VGAM288 is therefore inhibition of IL2-inducible T-cell Kinase (ITK, Accession NM_005546), a gene which plays a role in t cell proliferation and differentiation. Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical con-

ditions associated with ITK. The function of ITK has been established by previous studies. Signal transduction through the T-cell receptor (TCR; OMIM Ref. No. 186880) and cytokine receptors on the surface of T lymphocytes occurs largely via tyrosine phosphorylation of intracellular substrates. Signal transduction is thought to occur via association of these receptors with intracellular protein tyrosine kinases. To identify unique T-cell tyrosine kinases, Gibson et al. (1993) used PCR-based cloning with degenerate oligonucleotides directed at highly conserved motifs of tyrosine kinase domains. In this way, they cloned the complete cDNA for a unique human tyrosine kinase that is expressed mainly in T lymphocytes and natural killer (NK) cells. The cDNA predicted an open reading frame of 1,866 bp encoding a protein with a predicted size of 72 kD, which was in keeping with its size on Western blotting. A single 6.2-kb mRNA and 72-kD protein were detected in T lymphocytes and NK-like cell lines, but were not detected in other cell lineages. Sequence comparisons suggested that the protein is probably the human homolog of a murine interleukin-2-inducible T-cell kinase (ITK). However, unlike ITK, the message and protein levels for the new entity did not vary markedly on stimulation of human

IL-2 responsive T cells with IL-2. They referred to the gene and its protein product as EMT ('expressed mainly in T cells'). They concluded that EMT is a member of a new family of intracellular kinases that includes BPK (the kinase mutant in X-linked agammaglobulinemia, 300300). The expression of EMT message and protein in thymocytes and mature T cells, combined with its homology to BPK and its chromosomal localization, suggested that EMT may play a role in thymic ontogeny and growth regulation of mature T cells. Integrin adhesion receptors mediate critical interactions of T cells with other cells and extracellular matrix components during trafficking, as well as during antigen-specific recognition events in tissue. Phosphatidylinositol 3-kinase (PI3K; OMIM Ref. No. 601232) has a role in the regulation of integrin activity by CD3 (see OMIM Ref. No. 186790)-TCR and in the regulation of ITK. Woods et al. (2001) determined that TCR-mediated activation of beta-1 integrins (see OMIM Ref. No. ITGB1; 135630) requires activation of ITK and PI3K-dependent recruitment of ITK to detergent-insoluble glycosphingolipid-enriched microdomains (DIGs) via binding of the pleckstrin homology domain of ITK to the PI3K product PI(3,4,5)-P3. Likewise, activation of PI3K and

LCK (OMIM Ref. No. 153390) via CD4 (OMIM Ref. No. 186940) coreceptor stimulation can initiate beta-1 integrin activation dependent on ITK function. CD4 stimulation, together with targeting of ITK to DIGs, also activates TCR-independent beta-1 integrin function. Changes in beta-1 integrin function mediated by TCR-induced activation of ITK are accompanied by ITK-dependent modulation of the actin cytoskeleton. Woods et al. (2001) concluded that TCR-mediated activation of beta-1 integrin involves membrane relocalization and activation of ITK via coordinate action of PI3K and an SRC family tyrosine kinase. Animal model experiments lend further support to the function of ITK. By homologous recombination, Schaeffer et al. (1999) disrupted the Rlk (TXK; 600058) gene in mice. Heterozygotes were completely normal. Homozygous null Rlk mice showed increased amounts of Itk mRNA. The authors hypothesized that upregulation of related Tec kinases may partially compensate for the lack of Rlk. Schaeffer et al. (1999) therefore generated Rlk $-/-$ Itk $-/-$ mice by interbreeding. Itk-deficient mice have reduced numbers of mature T cells, particularly CD4⁺ cells, causing a decreased CD4-to-CD8 ratio. Rlk $-/-$ Itk $-/-$ mutants, however, had normal T cell numbers. Both CD4⁺

and CD8⁺ cell numbers are increased relative to Itk ^{-/-} mice. The persistent abnormal ratio of CD4⁺ to CD8⁺ cells suggested an altered regulation of lymphoid development and homeostasis in the double mutants. The double mutants had marked defects in T-cell receptor responses including proliferation, cytokine production, and apoptosis in vitro and adaptive immune responses to *Toxoplasma gondii* in vivo. Molecular events immediately downstream from the T-cell receptor were intact in Rlk ^{-/-} Itk ^{-/-} cells, but intermediate events including inositol trisphosphate production, calcium mobilization, and mitogen-activated protein kinase activation were impaired, establishing Tec kinases as critical regulators of T-cell receptor signaling required for phospholipase C-γ activation.

[15982] It is appreciated that the abovementioned animal model for ITK is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[15983] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15984] Schaeffer, E. M.; Debnath, J.; Yap, G.; McVicar, D.; Liao, X.

C.; Littman, D. R.; Sher, A.; Varmus, H. E.; Lenardo, M. J.; Schwartzberg, P. L. : Requirement for Tec kinases Rlk and Itk in T cell receptor signaling and immunity. Science 284: 638–641, 1999. ; and

[15985] Woods, M. L.; Kivens, W. J.; Adelsman, M. A.; Qiu, Y.; August, A.; Shimizu, Y. : A novel function for the Tec family tyrosine kinase Itk in activation of beta-1 integrins by the T-cell.

[15986] Further studies establishing the function and utilities of ITK are found in John Hopkins OMIM database record ID 186973, and in cited publications numbered 1133–1137 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Melatonin Receptor 1A (MTNR1A, Accession NM_005958) is another VGAM288 host target gene. MTNR1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTNR1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTNR1A BINDING SITE, designated SEQ ID:12582, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15987] Another function of VGAM288 is therefore inhibition of Melatonin Receptor 1A (MTNR1A, Accession NM_005958), a gene which likely mediates the reproductive and circadian actions of melatonin. Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTNR1A. The function of MTNR1A has been established by previous studies. Reppert and Weaver (1995) reviewed the hormonal properties of melatonin and the characteristics of the melatonin receptors. Brzezinski (1997) likewise gave a comprehensive review of the function of melatonin and its clinical implications. Sleep disruption, nightly restlessness, sundowning, and other circadian disturbances are frequently seen in Alzheimer disease (AD; 104300) patients. Since melatonin is the main endocrine message for circadian rhythmicity from the pineal, Liu et al. (1999) studied melatonin levels in the cerebrospinal fluid (CSF) of 85 AD patients and 82 age-matched controls. In old control subjects (older than 80 years of age), CSF melatonin levels were half those of control subjects 41 to 80 years of age. In AD patients the CSF melatonin levels were only one-fifth of those in control subjects. The authors did not find a diurnal rhythm in CSF melatonin levels in control

subjects or AD patients Von Gall et al. (2002) demonstrated that cycling expression of the clock gene Period-1 (OMIM Ref. No. 602260) in rodent pituitary cells depends on the heterologous sensitization of the adenosine A2B receptor (OMIM Ref. No. 600446), which occurs through the nocturnal activation of melatonin mt1 receptors. Eliminating the impact of the neurohormone melatonin simultaneously suppresses the expression of Period-1 and evokes an increase in the release of pituitary prolactin. Von Gall et al. (2002) concluded that their observations expose a mechanism by which 2 convergent signals interact within a temporal dimension to establish high-amplitude, precise, and robust cycles of gene expression.

[15988] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[15989] von Gall, C.; Garabette, M. L.; Kell, C. A.; Frenzel, S.; Dehghani, F.; Schumm-Draeger, P.-M.; Weaver, D. R.; Korf, H.-W.; Hastings, M. H.; Stehle, J. H. : Rhythmic gene expression in pituitary depends on heterologous sensitization by the neurohormone melatonin. *Nature Neurosci.* 5: 234-238, 2002. ; and

[15990] Weaver, D. R.; Rivkees, S. A.; Carlson, L. L.; Reppert, S. M. :

Localization of melatonin receptors in mammalian brain.In: Klein, D. C.; Moore, R. Y.; Reppert, S. M. : Suprachiasmatic.

[15991] Further studies establishing the function and utilities of MTNR1A are found in John Hopkins OMIM database record ID 600665, and in cited publications numbered 8179–8183, 812 and 10227 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.Oligophrenin 1 (OPHN1, Accession NM_002547) is another VGAM288 host target gene. OPHN1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by OPHN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPHN1 BINDING SITE, designated SEQ ID:8405, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15992] Another function of VGAM288 is therefore inhibition of Oligophrenin 1 (OPHN1, Accession NM_002547). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with OPHN1. Recombination Activating Gene 1 (RAG1, Accession NM_000448) is another VGAM288 host target gene. RAG1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAG1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAG1 BINDING SITE, designated SEQ ID:6040, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15993] Another function of VGAM288 is therefore inhibition of Recombination Activating Gene 1 (RAG1, Accession NM_000448). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAG1. Solute Carrier Family 18 (vesicular acetylcholine), Member 3 (SLC18A3, Accession NM_003055) is another VGAM288 host target gene. SLC18A3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SLC18A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of SLC18A3 BINDING SITE, designated SEQ ID:9019, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15994] Another function of VGAM288 is therefore inhibition of Solute Carrier Family 18 (vesicular acetylcholine), Member 3 (SLC18A3, Accession NM_003055). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC18A3. Aquaporin 10 (AQP10, Accession NM_080429) is another VGAM288 host target gene. AQP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AQP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP10 BINDING SITE, designated SEQ ID:27840, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15995] Another function of VGAM288 is therefore inhibition of Aquaporin 10 (AQP10, Accession NM_080429). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with AQP10. BTB (POZ) Domain Containing 3 (BTBD3, Accession NM_014962) is another VGAM288 host target gene. BTBD3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTBD3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTBD3 BINDING SITE, designated SEQ ID:17341, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15996] Another function of VGAM288 is therefore inhibition of BTB (POZ) Domain Containing 3 (BTBD3, Accession NM_014962). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTBD3. DRCTNNB1A (Accession NM_032581) is another VGAM288 host target gene. DRCTNNB1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DRCTNNB1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DRCTNNB1A BINDING SITE, des-

ignated SEQ ID:26316, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15997] Another function of VGAM288 is therefore inhibition of DRCTNNB1A (Accession NM_032581). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DRCTNNB1A. FLJ10700 (Accession NM_018182) is another VGAM288 host target gene. FLJ10700 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10700, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10700 BINDING SITE, designated SEQ ID:20021, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15998] Another function of VGAM288 is therefore inhibition of FLJ10700 (Accession NM_018182). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10700. FLJ23053 (Accession NM_022907) is another VGAM288 host target gene. FLJ23053 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ23053, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23053 BINDING SITE, designated SEQ ID:23207, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[15999] Another function of VGAM288 is therefore inhibition of FLJ23053 (Accession NM_022907). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23053. FLJ30663 (Accession XM_086046) is another VGAM288 host target gene. FLJ30663 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30663, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30663 BINDING SITE, designated SEQ ID:38462, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16000] Another function of VGAM288 is therefore inhibition of

FLJ30663 (Accession XM_086046). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30663. Glycoprotein V (platelet) (GP5, Accession NM_004488) is another VGAM288 host target gene. GP5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GP5 BINDING SITE, designated SEQ ID:10818, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16001] Another function of VGAM288 is therefore inhibition of Glycoprotein V (platelet) (GP5, Accession NM_004488). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GP5. Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571) is another VGAM288 host target gene. HEYL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HEYL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HEYL BINDING SITE, designated SEQ ID:15931, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16002] Another function of VGAM288 is therefore inhibition of Hairy/enhancer-of-split Related with YRPW Motif-like (HEYL, Accession NM_014571). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HEYL. KIAA0254 (Accession NM_014758) is another VGAM288 host target gene. KIAA0254 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0254, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0254 BINDING SITE, designated SEQ ID:16507, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16003] Another function of VGAM288 is therefore inhibition of KIAA0254 (Accession NM_014758). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0254. KIAA0447 (Accession XM_049733) is another VGAM288 host target gene. KIAA0447 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0447 BINDING SITE, designated SEQ ID:35495, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16004] Another function of VGAM288 is therefore inhibition of KIAA0447 (Accession XM_049733). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0447. KIAA0547 (Accession NM_014793) is another VGAM288 host target gene. KIAA0547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0547 BINDING SITE, designated SEQ ID:16696, to the

nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16005] Another function of VGAM288 is therefore inhibition of KIAA0547 (Accession NM_014793). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0547. KIAA0892 (Accession XM_048457) is another VGAM288 host target gene. KIAA0892 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0892, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0892 BINDING SITE, designated SEQ ID:35171, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16006] Another function of VGAM288 is therefore inhibition of KIAA0892 (Accession XM_048457). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0892. KIAA1223 (Accession XM_048747) is another VGAM288 host target gene. KIAA1223 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1223, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1223 BINDING SITE, designated SEQ ID:35249, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16007] Another function of VGAM288 is therefore inhibition of KIAA1223 (Accession XM_048747). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1223. KIAA1354 (Accession XM_027604) is another VGAM288 host target gene. KIAA1354 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1354, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1354 BINDING SITE, designated SEQ ID:30540, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16008] Another function of VGAM288 is therefore inhibition of KIAA1354 (Accession XM_027604). Accordingly, utilities

of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1354. MGC14859 (Accession XM_030295) is another VGAM288 host target gene. MGC14859 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC14859, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC14859 BINDING SITE, designated SEQ ID:31006, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16009] Another function of VGAM288 is therefore inhibition of MGC14859 (Accession XM_030295). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC14859. Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635) is another VGAM288 host target gene. P2RX1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by P2RX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of P2RX1 BINDING SITE, designated SEQ ID:33358, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16010] Another function of VGAM288 is therefore inhibition of Purinergic Receptor P2X, Ligand-gated Ion Channel, 1 (P2RX1, Accession XM_040635). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P2RX1. Septin 3 (SEPT3, Accession NM_019106) is another VGAM288 host target gene. SEPT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEPT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEPT3 BINDING SITE, designated SEQ ID:21184, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16011] Another function of VGAM288 is therefore inhibition of Septin 3 (SEPT3, Accession NM_019106). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with SEPT3. LOC150095 (Accession XM_097805) is another VGAM288 host target gene. LOC150095 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150095, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150095 BINDING SITE, designated SEQ ID:41131, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16012] Another function of VGAM288 is therefore inhibition of LOC150095 (Accession XM_097805). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150095. LOC163915 (Accession XM_099567) is another VGAM288 host target gene. LOC163915 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163915, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC163915 BINDING SITE, designated SEQ ID:42100, to the nucleotide sequence of VGAM288 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:2999.

[16013] Another function of VGAM288 is therefore inhibition of LOC163915 (Accession XM_099567). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163915. LOC165568 (Accession XM_092674) is another VGAM288 host target gene. LOC165568 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC165568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165568 BINDING SITE, designated SEQ ID:40138, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16014] Another function of VGAM288 is therefore inhibition of LOC165568 (Accession XM_092674). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165568. LOC197285 (Accession XM_113752) is another VGAM288 host target gene. LOC197285 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197285, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC197285 BINDING SITE, designated SEQ ID:42413, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16015] Another function of VGAM288 is therefore inhibition of LOC197285 (Accession XM_113752). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197285. LOC256997 (Accession XM_170900) is another VGAM288 host target gene. LOC256997 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC256997, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256997 BINDING SITE, designated SEQ ID:45653, to the nucleotide sequence of VGAM288 RNA, herein designated VGAM RNA, also designated SEQ ID:2999.

[16016] Another function of VGAM288 is therefore inhibition of LOC256997 (Accession XM_170900). Accordingly, utilities of VGAM288 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC256997. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 289 (VGAM289) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16017] VGAM289 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM289 was detected is described hereinabove with reference to Figs. 1–8.

[16018] VGAM289 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16019] VGAM289 gene encodes a VGAM289 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM289 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM289 precursor RNA is designated SEQ

ID:275, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:275 is located at position 113982 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[16020] VGAM289 precursor RNA folds onto itself, forming VGAM289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16021] An enzyme complex designated DICER COMPLEX, `dices` the VGAM289 folded precursor RNA into VGAM289 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 43%) nucleotide sequence of VGAM289 RNA is designated SEQ ID:3000, and is provided hereinbelow with reference to the sequence

listing part.

[16022] VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM289 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16023] VGAM289 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM289 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM289 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16024] The complementary binding of VGAM289 RNA, herein designated VGAM RNA, to host target binding sites on VGAM289 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM289 host target RNA into VGAM289 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16025] It is appreciated that VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM289 host target genes. The mRNA of each one of this plurality of VGAM289 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM289 RNA, herein designated VGAM

RNA, and which when bound by VGAM289 RNA causes inhibition of translation of respective one or more VGAM289 host target proteins.

[16026] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM289 gene, herein designated VGAM GENE, on one or more VGAM289 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16027] It is yet further appreciated that a function of VGAM289 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM289 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM289 correlate with, and may be deduced from, the identity of the host target genes which VGAM289 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16028] Nucleotide sequences of the VGAM289 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM289 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM289 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM289 are further described hereinbelow with reference to Table 1.

[16029] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM289 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM289 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16030] As mentioned hereinabove with reference to Fig. 1, a function of VGAM289 gene, herein designated VGAM is

inhibition of expression of VGAM289 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM289 correlate with, and may be deduced from, the identity of the target genes which VGAM289 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16031] Chromosome X Open Reading Frame 6 (CXorf6, Accession NM_005491) is a VGAM289 host target gene. CXorf6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CXorf6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CXorf6 BINDING SITE, designated SEQ ID:11989, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16032] A function of VGAM289 is therefore inhibition of Chromosome X Open Reading Frame 6 (CXorf6, Accession NM_005491). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXorf6. Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463) is another VGAM289 host target gene. HNR-

PDL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HNRPDL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HNRPDL BINDING SITE, designated SEQ ID:11948, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16033] Another function of VGAM289 is therefore inhibition of Heterogeneous Nuclear Ribonucleoprotein D-like (HNRPDL, Accession NM_005463), a gene which binds to rna molecules that contain au-rich elements. Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HNRPDL. The function of HNRPDL and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM144. Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 3 Regulatory Factor 1 (SLC9A3R1, Accession XM_046932) is another VGAM289 host target gene. SLC9A3R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by SLC9A3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC9A3R1 BINDING SITE, designated SEQ ID:34864, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16034] Another function of VGAM289 is therefore inhibition of Solute Carrier Family 9 (sodium/hydrogen exchanger), Isoform 3 Regulatory Factor 1 (SLC9A3R1, Accession XM_046932), a gene which is the regulatory cofactor of the NHE3 (SLC9A3) sodium/hydrogen antiporter. Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC9A3R1. The function of SLC9A3R1 has been established by previous studies. Murthy et al. (1998) isolated SLC9A3R1, which they termed NHERF, by screening a fetal frontal cortex cDNA library using a yeast 2-hybrid system with merlin as bait. Northern blot analysis revealed that SLC9A3R1 is ubiquitously expressed, with highest levels in kidney, liver, and pancreas. Deletion and mutation analyses showed that SLC9A3R1 associates with the N terminus but not with the C terminus of merlin. SLC9A3R1

was also shown to bind to moesin and radixin at the N terminus, the region with the most homology to merlin. Using immunocytochemistry, Murthy et al. (1998) demonstrated that SLC9A3R1 colocalizes with moesin at the ruffling membrane, microvilli, and filopodia in HeLa cells. Animal model experiments lend further support to the function of SLC9A3R1. Shenolikar et al. (2002) found that targeted disruption of the mouse *Nherf1* gene eliminated *Nherf1* expression in kidney and other tissues of the mutant mice without altering *Nherf2* levels in these tissues. Heterozygous and homozygous deficient male mice maintained normal blood electrolytes but showed increased urinary excretion of phosphate when compared with homozygous wildtype animals. Although the overall levels of renal *Nherf1* targets, *Slc9a3* and sodium-phosphate transport-2 (*Npt2*; 182309), were unchanged in the mutant mice, immunocytochemistry showed that the *Npt2* protein was aberrantly localized at internal sites in the renal proximal tubule cells. The mislocalization of *Npt2* paralleled a reduction in the transporter protein in renal brush-border membranes isolated from the mutant mice. In contrast, *Slc9a3* was appropriately localized at the apical surface of proximal tubules in both wildtype and mu-

tant mice. These data suggested that NHERF1 plays a unique role in the apical targeting and/or trafficking of NPT2 in the mammalian kidney, a function not shared by NHERF2 or other renal PDZ proteins. Phosphate wasting seen in the Nherf1 homozygous null mice provided a novel experimental system for defining the role of PDZ adaptors in the hormonal control of ion transport and renal disease

[16035] It is appreciated that the abovementioned animal model for SLC9A3R1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16036] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16037] Shenolikar, S.; Voltz, J. W.; Minkoff, C. M.; Wade, J. B.; Weinman, E. J. : Targeted disruption of the mouse NHERF-1 gene promotes internalization of proximal tubule sodium-phosphate cotransporter type IIa and renal phosphate wasting. Proc. Nat. Acad. Sci. 99: 11470-11475, 2002. ; and

[16038] Murthy, A.; Gonzalez-Agosti, C.; Cordero, E.; Pinney, D.; Candia, C.; Solomon, F.; Gusella, J.; Ramesh, V. : NHE-RF,

a regulatory cofactor for Na(+)-H(+) exchange, is a common interactor f.

[16039] Further studies establishing the function and utilities of SLC9A3R1 are found in John Hopkins OMIM database record ID 604990, and in cited publications numbered 434 and 7098-7100 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926) is another VGAM289 host target gene. ZFP36L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP36L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP36L1 BINDING SITE, designated SEQ ID:11361, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16040] Another function of VGAM289 is therefore inhibition of Zinc Finger Protein 36, C3H Type-like 1 (ZFP36L1, Accession NM_004926), a gene which is a regulatory protein involved in regulating the response to growth factors. Accordingly, utilities of VGAM289 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with ZFP36L1. The function of ZFP36L1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. ARHGAP10 (Accession NM_020824) is another VGAM289 host target gene. ARHGAP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGAP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGAP10 BINDING SITE, designated SEQ ID:21888, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16041] Another function of VGAM289 is therefore inhibition of ARHGAP10 (Accession NM_020824). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGAP10. GBTS1 (Accession NM_145173) is another VGAM289 host target gene. GBTS1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GBTS1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GBTS1 BINDING SITE, designated SEQ ID:29724, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16042] Another function of VGAM289 is therefore inhibition of GBTS1 (Accession NM_145173). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GBTS1. KIAA0547 (Accession NM_014793) is another VGAM289 host target gene. KIAA0547 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0547, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0547 BINDING SITE, designated SEQ ID:16694, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16043] Another function of VGAM289 is therefore inhibition of KIAA0547 (Accession NM_014793). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0547. MEGF10 (Accession NM_032446) is another VGAM289 host target gene. MEGF10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MEGF10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MEGF10 BINDING SITE, designated SEQ ID:26207, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16044] Another function of VGAM289 is therefore inhibition of MEGF10 (Accession NM_032446). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MEGF10. LOC146455 (Accession XM_085471) is another VGAM289 host target gene. LOC146455 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146455, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146455 BINDING SITE, designated SEQ ID:38154, to the nucleotide se-

quence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16045] Another function of VGAM289 is therefore inhibition of LOC146455 (Accession XM_085471). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146455. LOC204084 (Accession XM_115181) is another VGAM289 host target gene. LOC204084 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC204084, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204084 BINDING SITE, designated SEQ ID:43085, to the nucleotide sequence of VGAM289 RNA, herein designated VGAM RNA, also designated SEQ ID:3000.

[16046] Another function of VGAM289 is therefore inhibition of LOC204084 (Accession XM_115181). Accordingly, utilities of VGAM289 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204084. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 290 (VGAM290) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16047] VGAM290 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM290 was detected is described hereinabove with reference to Figs. 1–8.

[16048] VGAM290 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16049] VGAM290 gene encodes a VGAM290 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM290 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM290 precursor RNA is designated SEQ ID:276, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:276 is located at position 108012 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16050] VGAM290 precursor RNA folds onto itself, forming VGAM290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16051] An enzyme complex designated DICER COMPLEX, `dices` the VGAM290 folded precursor RNA into VGAM290 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM290 RNA is designated SEQ ID:3001, and is provided hereinbelow with reference to the sequence listing part.

[16052] VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM290 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM290 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16053] VGAM290 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM290 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM290 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16054] The complementary binding of VGAM290 RNA, herein designated VGAM RNA, to host target binding sites on VGAM290 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM290 host target RNA into VGAM290 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16055] It is appreciated that VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM290 host target genes. The mRNA of each one of this plurality of VGAM290 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM290 RNA, herein designated VGAM RNA, and which when bound by VGAM290 RNA causes inhibition of translation of respective one or more VGAM290 host target proteins.

[16056] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM290 gene, herein designated VGAM GENE, on one or more VGAM290 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16057] It is yet further appreciated that a function of VGAM290 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM290 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM290 correlate with, and may be deduced

from, the identity of the host target genes which VGAM290 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16058] Nucleotide sequences of the VGAM290 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM290 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM290 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM290 are further described hereinbelow with reference to Table 1.

[16059] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM290 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM290 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16060] As mentioned hereinabove with reference to Fig. 1, a function of VGAM290 gene, herein designated VGAM is inhibition of expression of VGAM290 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM290 correlate with, and may be deduced from, the identity of the target genes which VGAM290

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16061] Radixin (RDX, Accession NM_002906) is a VGAM290 host target gene. RDX BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RDX, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RDX BINDING SITE, designated SEQ ID:8808, to the nucleotide sequence of VGAM290 RNA, herein designated VGAM RNA, also designated SEQ ID:3001.

[16062] A function of VGAM290 is therefore inhibition of Radixin (RDX, Accession NM_002906), a gene which plays a crucial role in the binding of the barbed end of actin filaments to the plasma membrane. Accordingly, utilities of VGAM290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RDX. The function of RDX has been established by previous studies. Radixin is a cytoskeletal protein that may be important in linking actin to the plasma membrane. Cloning of the murine and porcine radixin cDNAs demonstrated a protein highly homologous to ezrin (OMIM Ref. No. 123900) and moesin (OMIM Ref. No. 309845). Wilgenbus et al. (1993) cloned

and sequenced the human radixin cDNA and found the predicted amino acid sequence for the human protein to be nearly identical to those predicted for radixin in the two other species. Animal model experiments lend further support to the function of RDX. The ezrin–radixin–moesin (ERM) family of proteins crosslink actin filaments and integral membrane proteins. Radixin (encoded by Rdx) is the dominant ERM protein in the liver of wildtype mice and is concentrated at bile canalicular membranes (BCM).

Kikuchi et al. (2002) showed that Rdx $-/-$ mice are normal at birth, but their serum concentrations of conjugated bilirubin begin to increase gradually around 4 weeks of age, and they show mild liver injury after 8 weeks. This phenotype is similar to human conjugated hyperbilirubinemia in Dubin–Johnson syndrome (OMIM Ref. No. 237500), which is caused by mutations in the ABCC2 gene (OMIM Ref. No. 601107), although Dubin–Johnson syndrome is not associated with overt liver injury. In wildtype mice, the protein product of the ABCC2 gene, multidrug resistance protein–2, or MRP2, concentrates at BCMs to secrete conjugated bilirubin into bile. In the BCMs of Rdx $-/-$ mice, Mrp2 is decreased compared with other BCM proteins such as dipeptidyl peptidase IV (CD26; 102720)

and P-glycoproteins. In vitro binding studies showed that radixin associates directly with the carboxy-terminal cytoplasmic domain of human MRP2. These findings indicated that radixin is required for secretion of conjugated bilirubin through its support of Mrp2 localization at BCMs.

[16063] It is appreciated that the abovementioned animal model for RDX is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16064] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16065] Wilgenbus, K. K.; Milatovich, A.; Francke, U.; Furthmayr, H. : Molecular cloning, cDNA sequence, and chromosomal assignment of the human radixin gene and two dispersed pseudogenes. *Genomics* 16: 199–206, 1993. ; and

[16066] Kikuchi, S.; Hata, M.; Fukumoto, K.; Yamane, Y.; Matsui, T.; Tamura, A.; Yonemura, S.; Yamagishi, H.; Keppler, D.; Tsukita, S.; Tsukita, S. : Radixin deficiency causes conjugated hyperbi.

[16067] Further studies establishing the function and utilities of RDX are found in John Hopkins OMIM database record ID 179410, and in cited publications numbered 2716–2717

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083) is another VGAM290 host target gene. XK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by XK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of XK BINDING SITE, designated SEQ ID:22062, to the nucleotide sequence of VGAM290 RNA, herein designated VGAM RNA, also designated SEQ ID:3001.

[16068] Another function of VGAM290 is therefore inhibition of Kell Blood Group Precursor (McLeod phenotype) (XK, Accession NM_021083). Accordingly, utilities of VGAM290 include diagnosis, prevention and treatment of diseases and clinical conditions associated with XK. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 291 (VGAM291) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16069] VGAM291 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM291 was detected is described hereinabove with reference to Figs. 1–8.

[16070] VGAM291 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16071] VGAM291 gene encodes a VGAM291 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM291 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM291 precursor RNA is designated SEQ ID:277, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:277 is located at position 95193 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16072] VGAM291 precursor RNA folds onto itself, forming VGAM291 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16073] An enzyme complex designated DICER COMPLEX, `dices` the VGAM291 folded precursor RNA into VGAM291 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM291 RNA is designated SEQ ID:3002, and is provided hereinbelow with reference to the sequence listing part.

[16074] VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM291 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[16075] VGAM291 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM291 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM291 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16076] The complementary binding of VGAM291 RNA, herein designated VGAM RNA, to host target binding sites on VGAM291 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM291 host target RNA into VGAM291 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16077] It is appreciated that VGAM291 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM291 host target genes. The mRNA of each one of this plurality of VGAM291 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM291 RNA, herein designated VGAM RNA, and which when bound by VGAM291 RNA causes inhibition of translation of respective one or more VGAM291 host target proteins.

[16078] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM291 gene, herein designated VGAM GENE, on one or more VGAM291 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16079] It is yet further appreciated that a function of VGAM291 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM291 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM291 correlate with, and may be deduced from, the identity of the host target genes which VGAM291 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16080] Nucleotide sequences of the VGAM291 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM291 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM291 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM291 are further
described hereinbelow with reference to Table 1.

[16081] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM291 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM291 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[16082] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM291 gene, herein designated VGAM is
inhibition of expression of VGAM291 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM291 correlate with, and may be deduced
from, the identity of the target genes which VGAM291
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[16083] Angiopoietin 1 (ANGPT1, Accession NM_139290) is a
VGAM291 host target gene. ANGPT1 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ANGPT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ANGPT1 BINDING SITE, designated SEQ ID:29289, to the nucleotide sequence of VGAM291 RNA, herein designated VGAM RNA, also designated SEQ ID:3002.

[16084] A function of VGAM291 is therefore inhibition of Angiopoietin 1 (ANGPT1, Accession NM_139290), a gene which binds and activates tie2 receptor by inducing its tyrosine phosphorylation. Accordingly, utilities of VGAM291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ANGPT1. The function of ANGPT1 has been established by previous studies. By FISH and radiation hybrid analysis, Cheung et al. (1998) mapped the ANGPT1 gene to 8q22.3-q23. By FISH, Valenzuela et al. (1999) mapped the ANGPT1 gene to 8q22 in a region that shows homology of synteny to mouse chromosome 15, where they mapped the mouse Angpt1 gene. However, by indirect in situ PCR and FISH, Marziliano et al. (1999) mapped the Angpt1 gene in the mouse to chromosome 9E2. To explore the possibility that VEGF and an-

giopietins collaborate during tumor angiogenesis, Holash et al. (1999) analyzed several different murine and human tumor models. The apparent association of tumor vessel regression, apoptosis, and disruption of endothelial cell interactions with support cells in rat C6 gliomas raised the possibility that blockade of the stabilizing action of Ang1 might be contributing to tumor vessel regression. Consistent with this possibility, Holash et al. (1999) noted that angiopoietin-1 was antiapoptotic for cultured endothelial cells and expression of its antagonist angiopoietin-2 was induced in the endothelium of co-opted tumor vessels before their regression. Diffuse angiopoietin-1 expression in human tumors resembled that seen in the rat model. Holash et al. (1999) suggested that a subset of tumors rapidly co-opts existing host vessels to form an initially well vascularized tumor mass. Perhaps as part of a host defense mechanism there is widespread regression of these initially co-opted vessels, leading to a secondarily avascular tumor and a massive tumor cell loss. However, the remaining tumor is ultimately rescued by robust angiogenesis at the tumor margin. Animal model experiments lend further support to the function of ANGPT1. Suri et al. (1996) showed that mice engineered to lack an-

angiopoietin-1 display angiogenic defects reminiscent of those previously seen in mice lacking Tie2, demonstrating that angiopoietin-1 is a primary physiologic ligand for Tie2 and that it has critical in vivo angiogenic actions that are distinct from vascular endothelial growth factor (VEGF; 192240) and that are not reflected in the classic in vitro assays used to characterize VEGF. They concluded that angiopoietin-1 appears to play a crucial role in mediating reciprocal interactions between the endothelium and surrounding matrix and mesenchyme.

[16085] It is appreciated that the abovementioned animal model for ANGPT1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16086] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16087] Holash, J.; Maisonpierre, P. C.; Compton, D.; Boland, P.; Alexander, C. R.; Zagzag, D.; Yancopoulos, G. D.; Wiegand, S. J. : Vessel cooption, regression, and growth in tumors mediated by angiopoietins and VEGF. Science 284: 1994-1998, 1999. ; and

[16088] Suri, C.; Jones, P. F.; Patan, S.; Bartunkova, S.; Maison-

pierre, P. C.; Davis, S.; Sato, T. N.; Yancopoulos, G. D. :
Requisite role of angiopoietin-1, a ligand for the TIE2 receptor, du.

[16089] Further studies establishing the function and utilities of ANGPT1 are found in John Hopkins OMIM database record ID 601667, and in cited publications numbered 9394-9396, 10441, 9397-9400, 1045 and 10205 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 2 (facilitated glucose transporter), Member 3 (SLC2A3, Accession NM_006931) is another VGAM291 host target gene. SLC2A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC2A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC2A3 BINDING SITE, designated SEQ ID:13815, to the nucleotide sequence of VGAM291 RNA, herein designated VGAM RNA, also designated SEQ ID:3002.

[16090] Another function of VGAM291 is therefore inhibition of Solute Carrier Family 2 (facilitated glucose transporter), Member 3 (SLC2A3, Accession NM_006931), a gene which

probably is a neuronal glucose transporter. Accordingly, utilities of VGAM291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC2A3. The function of SLC2A3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247.FLJ13110 (Accession NM_022912) is another VGAM291 host target gene. FLJ13110 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13110, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13110 BINDING SITE, designated SEQ ID:23219, to the nucleotide sequence of VGAM291 RNA, herein designated VGAM RNA, also designated SEQ ID:3002.

[16091] Another function of VGAM291 is therefore inhibition of FLJ13110 (Accession NM_022912). Accordingly, utilities of VGAM291 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13110. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present inven-

tion, referred to here as Viral Genomic Address Messenger 292 (VGAM292) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16092] VGAM292 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM292 was detected is described hereinabove with reference to Figs. 1–8.

[16093] VGAM292 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16094] VGAM292 gene encodes a VGAM292 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM292 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM292 precursor RNA is designated SEQ ID:278, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:278 is located at position 9896 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16095] VGAM292 precursor RNA folds onto itself, forming VGAM292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16096] An enzyme complex designated DICER COMPLEX, `dices` the VGAM292 folded precursor RNA into VGAM292 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 53%) nucleotide sequence of VGAM292 RNA is designated SEQ ID:3003, and is provided hereinbelow with reference to the sequence listing part.

[16097] VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM292 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM292 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16098] VGAM292 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM292 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM292 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16099] The complementary binding of VGAM292 RNA, herein designated VGAM RNA, to host target binding sites on VGAM292 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM292 host target RNA into VGAM292 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16100] It is appreciated that VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM292 host target genes. The mRNA of each one of this plurality of VGAM292 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM292 RNA, herein designated VGAM RNA, and which when bound by VGAM292 RNA causes inhibition of translation of respective one or more VGAM292 host target proteins.

[16101] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM292 gene, herein designated VGAM GENE, on one or more VGAM292 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16102] It is yet further appreciated that a function of VGAM292 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM292 correlate with, and may be deduced

from, the identity of the host target genes which VGAM292 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16103] Nucleotide sequences of the VGAM292 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM292 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM292 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM292 are further described hereinbelow with reference to Table 1.

[16104] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM292 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM292 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16105] As mentioned hereinabove with reference to Fig. 1, a function of VGAM292 gene, herein designated VGAM is inhibition of expression of VGAM292 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM292 correlate with, and may be deduced from, the identity of the target genes which VGAM292

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16106] Acidic Repeat Containing (ACRC, Accession NM_052957) is a VGAM292 host target gene. ACRC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACRC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACRC BINDING SITE, designated SEQ ID:27517, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16107] A function of VGAM292 is therefore inhibition of Acidic Repeat Containing (ACRC, Accession NM_052957). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACRC. Aldehyde Dehydrogenase 3 Family, Member A2 (ALDH3A2, Accession XM_045060) is another VGAM292 host target gene. ALDH3A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH3A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

complementarity of the nucleotide sequences of ALDH3A2 BINDING SITE, designated SEQ ID:34340, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16108] Another function of VGAM292 is therefore inhibition of Aldehyde Dehydrogenase 3 Family, Member A2 (ALDH3A2, Accession XM_045060). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH3A2. Forkhead Box F1 (FOXF1, Accession NM_001451) is another VGAM292 host target gene. FOXF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXF1 BINDING SITE, designated SEQ ID:7183, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16109] Another function of VGAM292 is therefore inhibition of Forkhead Box F1 (FOXF1, Accession NM_001451), a gene which is a probable transcription activator for a number of lung-specific genes. Accordingly, utilities of VGAM292

include diagnosis, prevention and treatment of diseases and clinical conditions associated with FOXF1. The function of FOXF1 has been established by previous studies. The forkhead genes are transcription factors distinguished by a characteristic 100–amino acid motif that was originally identified in *Drosophila* (see OMIM Ref. No. 164874). Pierrou et al. (1994) identified 7 human genes containing forkhead domains and designated them forkhead related activators (FREAC) 1 through 7. Northern blot analysis revealed that the FREAC1, or FKHL5, gene is expressed as a 2.6–kb mRNA in placenta and adult and fetal lung. Hellqvist et al. (1996) reported the FREAC1 cDNA sequence. The predicted 354–amino acid protein is nearly identical to FREAC2 (FKHL6; 603250) within a 112–residue region containing the forkhead domain and adjacent sequences, and within the C–terminal region. Using a reporter gene construct containing FREAC2 binding sequences in the promoter, Hellqvist et al. (1996) demonstrated that both FREAC1 and FREAC2 have C–terminal transcriptional activation domains. FREAC1/FREAC2 binding sequences are present in the promoters of several lung–specific genes, including CC10 (OMIM Ref. No. 192020) and SPB (SFTPB; 178640). While both FREAC1 and FREAC2 transactivated

an SPB promoter construct, CC10 was activated only by FREAC1. CC10 activation occurred specifically in a lung cell line with Clara cell-like characteristics. Hellqvist et al. (1996) reported that the mouse HFH8 gene and FREAC1 share 90% nucleotide sequence identity. By resequencing of HFH8, these authors demonstrated that 5 frameshifts in the HFH8 sequence reported by Clevidence et al. (1994) were due to sequencing errors.

[16110] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16111] Clevidence, D. E.; Overdier, D. G.; Peterson, R. S.; Porcella, A.; Ye, H.; Paulson, K. E.; Costa, R. H. : Members of the HNF-3/forkhead family of transcription factors exhibit distinct cellular expression patterns in lung and regulate the surfactant protein B promoter. Dev. Biol. 166: 195-209, 1994. ; and

[16112] Hellqvist, M.; Mahlapuu, M.; Blixt, A.; Enerback, S.; Carlsson, P. : The human forkhead protein FREAC-2 contains two functionally redundant activation domains and interacts with TBP and.

[16113] Further studies establishing the function and utilities of FOXF1 are found in John Hopkins OMIM database record

ID 601089, and in cited publications numbered 9456–9460 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Growth Arrest–specific 11 (GAS11, Accession NM_001481) is another VGAM292 host target gene. GAS11 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GAS11, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAS11 BINDING SITE, designated SEQ ID:7220, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16114] Another function of VGAM292 is therefore inhibition of Growth Arrest–specific 11 (GAS11, Accession NM_001481). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAS11. NCSTN (Accession XM_057331) is another VGAM292 host target gene. NCSTN BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by NCSTN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of NCSTN BINDING SITE, designated SEQ ID:36507, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16115] Another function of VGAM292 is therefore inhibition of NCSTN (Accession XM_057331), a gene which has a central role in presenilin-mediated processing of beta-amyloid precursor protein (beta-APP, MIM 104760) and some aspects of notch (MIM 190198)/glp-1 signaling in vivo. Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCSTN. The function of NCSTN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM152.Prostaglandin-endoperoxide Synthase 2 (prostaglandin G/H synthase and cyclooxygenase) (PTGS2, Accession NM_000963) is another VGAM292 host target gene. PTGS2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PTGS2 BINDING SITE, designated SEQ ID:6683, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16116] Another function of VGAM292 is therefore inhibition of Prostaglandin–endoperoxide Synthase 2 (prostaglandin G/H synthase and cyclooxygenase) (PTGS2, Accession NM_000963), a gene which may have a role as a major mediator of inflammation and/or a role for prostanoid signaling in activity–dependent plasticity. Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTGS2. The function of PTGS2 has been established by previous studies. Inflammation causes the induction of COX2, leading to the release of prostanoids, which sensitize peripheral nociceptor terminals and produce localized pain hypersensitivity. Peripheral inflammation also generates pain hypersensitivity in neighboring uninjured tissue, because of the increased neuronal excitability in the spinal cord, and a syndrome comprising diffuse muscle and joint pain, fever, lethargy, and anorexia. Samad et al. (2001) showed that COX2 may be involved in central ner–

vous system (CNS) responses, by finding a widespread induction of COX2 expression in spinal cord neurons and in other regions of the CNS, elevating prostaglandin E2 (PGE2) levels in the cerebrospinal fluid. The major inducer of central COX2 upregulation is IL1-beta in the CNS, and as basal phospholipase A2 (see OMIM Ref. No. 600522) activity in the CNS does not change with peripheral inflammation, COX2 levels must regulate central prostanoid production. In the rat, intraspinal administration of an interleukin-converting enzyme or COX2 inhibitor decreased inflammation-induced central PGE2 levels and mechanical hyperalgesia. Thus, Samad et al. (2001) concluded that preventing central prostanoid production by inhibiting the IL1-beta-mediated induction of COX2 in neurons or by inhibiting central COX2 activity reduces centrally generated inflammatory pain hypersensitivity. Animal model experiments lend further support to the function of PTGS2. Morham et al. (1995) noted that cyclooxygenase-2 (COX2) is induced at high levels in migratory and other responding cells by proinflammatory stimuli. COX2 is generally considered to be a mediator of inflammation. Its isoform, COX1, is constitutively expressed in most tissues and is thought to mediate 'housekeeping' functions. These

2 enzymes are therapeutic targets of the widely used non-steroidal antiinflammatory drugs (OMIM Ref. No. NSAIDs). To investigate further the different physiologic roles of these isoforms, Morham et al. (1995) used homologous recombination to disrupt the mouse gene encoding COX2 (Ptgs2). Mice lacking COX2 were found to have normal inflammatory responses to treatments with tetradecanoyl phorbol acetate or arachidonic acid. However, they developed severe nephropathy and were susceptible to peritonitis.

[16117] It is appreciated that the abovementioned animal model for PTGS2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16118] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16119] Morham, S. G.; Langenbach, R.; Loftin, C. D.; Tiano, H. F.; Vouloumanos, N.; Jennette, J. C.; Mahler, J. F.; Kluckman, K. D.; Ledford, A.; Lee, C. A.; Smithies, O. : Prostaglandin synthase 2 gene disruption causes severe renal pathology in the mouse. *Cell* 83: 473–482, 1995. ; and

[16120] Samad, T. A.; Moore, K. A.; Sapirstein, A.; Billet, S.; All–

chorne, A.; Poole, S.; Bonventre, J. V.; Woolf, C. J. : Inter-leukin-1-beta-mediated induction of Cox-2 in the CNS contributes.

[16121] Further studies establishing the function and utilities of PTGS2 are found in John Hopkins OMIM database record ID 600262, and in cited publications numbered 7932, 10848-7934, 10849-7937, 8080-8086, 10841, 11170, 8090-809 and 10887 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RNA Guanylyltransferase and 5'-phosphatase (RNGTT, Accession NM_003800) is another VGAM292 host target gene. RNGTT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNGTT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNGTT BINDING SITE, designated SEQ ID:9896, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16122] Another function of VGAM292 is therefore inhibition of RNA Guanylyltransferase and 5'-phosphatase (RNGTT, Accession NM_003800), a gene which is an mRNA capping

enzyme; bifunctional enzyme containing both 5'-triphosphatase and mRNA guanylyltransferase activity. Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNGTT. The function of RNGTT has been established by previous studies. Independently, both Tsukamoto et al. (1998) and Yamada-Okabe et al. (1998) cloned cDNAs encoding RNGTT, which they designated CAP1a and HCE1 (human capping enzyme-1), respectively. Using RT-PCR, Tsukamoto et al. (1998) demonstrated CAP1a expression in all human tissues tested. Yamada-Okabe et al. (1998) found that recombinant HCE1 protein displayed RNA 5-prime-triphosphatase and guanylyltransferase activities and formed a cap structure at the 5-prime-triphosphate end of RNA. These authors also identified HCE1A and HCE1B, alternatively spliced mRNAs encoding proteins lacking part of the C-terminal region. The shorter isoforms possessed only RNA 5-prime-triphosphatase activity. HCE1, but not HCE1A or HCE1B, complemented *S. cerevisiae* *ceg1* and *cet1* mutations. Yamada-Okabe et al. (1998) concluded that the N-terminal part of HCE1 is responsible for RNA 5-prime-triphosphatase activity and the C-terminal part

is essential for guanylyltransferase activity. RT-PCR analysis indicated that the level of HCE1 mRNA was significantly higher than those of HCE1A and HCE1B.

[16123] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16124] Tsukamoto, T.; Shibagaki, Y.; Murakoshi, T.; Suzuki, M.; Nakamura, A.; Gotoh, H.; Mizumoto, K. : Cloning and characterization of two human cDNAs encoding the mRNA capping enzyme. *Biochem. Biophys. Res. Commun.* 243: 101-108, 1998. ; and

[16125] Yamada-Okabe, T.; Doi, R.; Shimmi, O.; Arisawa, M.; Yamada-Okabe, H. : Isolation and characterization of a human cDNA for mRNA 5-prime-capping enzyme. *Nucleic Acids Res.* 26: 1700-1706, 1998.

[16126] Further studies establishing the function and utilities of RNGTT are found in John Hopkins OMIM database record ID 603512, and in cited publications numbered 1105-1108 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ATPase, Class II, Type 9A (ATP9A, Accession XM_030577) is another VGAM292 host target gene. ATP9A BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by ATP9A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP9A BINDING SITE, designated SEQ ID:31086, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16127] Another function of VGAM292 is therefore inhibition of ATPase, Class II, Type 9A (ATP9A, Accession XM_030577). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP9A. BDG-29 (Accession XM_051343) is another VGAM292 host target gene. BDG-29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BDG-29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BDG-29 BINDING SITE, designated SEQ ID:35814, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16128] Another function of VGAM292 is therefore inhibition of BDG-29 (Accession XM_051343). Accordingly, utilities of

VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BDG-29. CPR2 (Accession NM_030900) is another VGAM292 host target gene. CPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPR2 BINDING SITE, designated SEQ ID:25177, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16129] Another function of VGAM292 is therefore inhibition of CPR2 (Accession NM_030900). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPR2. DKFZp761D221 (Accession NM_032291) is another VGAM292 host target gene. DKFZp761D221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp761D221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DK-

FZp761D221 BINDING SITE, designated SEQ ID:26057, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16130] Another function of VGAM292 is therefore inhibition of DKFZp761D221 (Accession NM_032291). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp761D221. Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538) is another VGAM292 host target gene. ERMAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ERMAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ERMAP BINDING SITE, designated SEQ ID:20606, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16131] Another function of VGAM292 is therefore inhibition of Erythroblast Membrane-associated Protein (ERMAP, Accession NM_018538). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERMAP. F-box Only

Protein 5 (FBXO5, Accession NM_012177) is another VGAM292 host target gene. FBXO5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FBXO5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FBXO5 BINDING SITE, designated SEQ ID:14466, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16132] Another function of VGAM292 is therefore inhibition of F-box Only Protein 5 (FBXO5, Accession NM_012177). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FBXO5. FLJ10450 (Accession NM_018095) is another VGAM292 host target gene. FLJ10450 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10450 BINDING SITE, designated SEQ ID:19863, to the nucleotide sequence of VGAM292 RNA, herein designated

VGAM RNA, also designated SEQ ID:3003.

[16133] Another function of VGAM292 is therefore inhibition of FLJ10450 (Accession NM_018095). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10450. FLJ22009 (Accession XM_015700) is another VGAM292 host target gene. FLJ22009 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22009, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22009 BINDING SITE, designated SEQ ID:30244, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16134] Another function of VGAM292 is therefore inhibition of FLJ22009 (Accession XM_015700). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22009. KIAA1204 (Accession XM_045011) is another VGAM292 host target gene. KIAA1204 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1204, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1204 BINDING SITE, designated SEQ ID:34316, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16135] Another function of VGAM292 is therefore inhibition of KIAA1204 (Accession XM_045011). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1204. KIAA1458 (Accession XM_044434) is another VGAM292 host target gene. KIAA1458 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1458, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1458 BINDING SITE, designated SEQ ID:34206, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16136] Another function of VGAM292 is therefore inhibition of KIAA1458 (Accession XM_044434). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1458. MGC24447 (Accession NM_138288) is another VGAM292 host target gene. MGC24447 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC24447, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC24447 BINDING SITE, designated SEQ ID:28702, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16137] Another function of VGAM292 is therefore inhibition of MGC24447 (Accession NM_138288). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC24447. MST4 (Accession NM_016542) is another VGAM292 host target gene. MST4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MST4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MST4 BINDING SITE, designated SEQ ID:18610, to the nucleotide sequence of

VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16138] Another function of VGAM292 is therefore inhibition of MST4 (Accession NM_016542). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MST4. STRIN (Accession NM_016271) is another VGAM292 host target gene. STRIN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STRIN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STRIN BINDING SITE, designated SEQ ID:18396, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16139] Another function of VGAM292 is therefore inhibition of STRIN (Accession NM_016271). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STRIN. LOC145622 (Accession XM_085186) is another VGAM292 host target gene. LOC145622 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of

mRNA encoded by LOC145622, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145622 BINDING SITE, designated SEQ ID:37912, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16140] Another function of VGAM292 is therefore inhibition of LOC145622 (Accession XM_085186). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145622. LOC219401 (Accession XM_166706) is another VGAM292 host target gene. LOC219401 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC219401, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219401 BINDING SITE, designated SEQ ID:44596, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16141] Another function of VGAM292 is therefore inhibition of LOC219401 (Accession XM_166706). Accordingly, utilities

of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219401. LOC257443 (Accession XM_171072) is another VGAM292 host target gene. LOC257443 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC257443, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257443 BINDING SITE, designated SEQ ID:45874, to the nucleotide sequence of VGAM292 RNA, herein designated VGAM RNA, also designated SEQ ID:3003.

[16142] Another function of VGAM292 is therefore inhibition of LOC257443 (Accession XM_171072). Accordingly, utilities of VGAM292 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257443. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 293 (VGAM293) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16143] VGAM293 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM293 was detected is described hereinabove with reference to Figs. 1–8.

[16144] VGAM293 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16145] VGAM293 gene encodes a VGAM293 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM293 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM293 precursor RNA is designated SEQ ID:279, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:279 is located at position 23397 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16146] VGAM293 precursor RNA folds onto itself, forming VGAM293 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16147] An enzyme complex designated DICER COMPLEX, `dices` the VGAM293 folded precursor RNA into VGAM293 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM293 RNA is designated SEQ ID:3004, and is provided hereinbelow with reference to the sequence listing part.

[16148] VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM293 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[16149] VGAM293 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM293 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM293 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16150] The complementary binding of VGAM293 RNA, herein designated VGAM RNA, to host target binding sites on VGAM293 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM293 host target RNA into VGAM293 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16151] It is appreciated that VGAM293 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM293 host target genes. The mRNA of each one of this plurality of VGAM293 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM293 RNA, herein designated VGAM RNA, and which when bound by VGAM293 RNA causes inhibition of translation of respective one or more VGAM293 host target proteins.

[16152] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM293 gene, herein designated VGAM GENE, on one or more VGAM293 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16153] It is yet further appreciated that a function of VGAM293 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM293 correlate with, and may be deduced from, the identity of the host target genes which VGAM293 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16154] Nucleotide sequences of the VGAM293 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM293 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM293 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM293 are further
described hereinbelow with reference to Table 1.

[16155] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM293 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM293 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[16156] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM293 gene, herein designated VGAM is
inhibition of expression of VGAM293 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM293 correlate with, and may be deduced
from, the identity of the target genes which VGAM293
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[16157] HTRA3 (Accession XM_114416) is a VGAM293 host target
gene. HTRA3 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by HTRA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTRA3 BINDING SITE, designated SEQ ID:42944, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16158] A function of VGAM293 is therefore inhibition of HTRA3 (Accession XM_114416). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTRA3. Kallmann Syndrome 1 Sequence (KAL1, Accession NM_000216) is another VGAM293 host target gene. KAL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KAL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KAL1 BINDING SITE, designated SEQ ID:5720, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16159] Another function of VGAM293 is therefore inhibition of

Kallmann Syndrome 1 Sequence (KAL1, Accession NM_000216). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KAL1. Solute Carrier Family 6 (neurotransmitter transporter, betaine/GABA), Member 12 (SLC6A12, Accession NM_003044) is another VGAM293 host target gene. SLC6A12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC6A12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC6A12 BINDING SITE, designated SEQ ID:9011, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16160] Another function of VGAM293 is therefore inhibition of Solute Carrier Family 6 (neurotransmitter transporter, betaine/GABA), Member 12 (SLC6A12, Accession NM_003044), a gene which transports betaine and gaba. Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC6A12. The function of SLC6A12 has been established by previous studies. Yamauchi et al.

(1992) stated that Madin–Darby canine kidney (MDCK) cells accumulate betaine when cultured in hypertonic media. They isolated an MDCK cell cDNA encoding a renal betaine transporter and designated it BGT1. When expressed in *Xenopus* oocytes, the BGT1 protein exhibited chloride– and sodium–dependent transport of both betaine and the neurotransmitter GABA. Northern blot analysis revealed that BGT1 expression is limited to the canine kidney medulla and is induced in MDCK cells by hypertonicity. Using the canine BGT1 sequence, Rasola et al. (1995) isolated a cDNA from a kidney library encoding the human homolog. The predicted 614–amino acid human protein has the typical structure of neurotransmitter transporters, with 12 transmembrane domains and a large extracellular loop between the third and fourth transmembrane domains. Northern blot analysis indicated that BGT1 is expressed as several mRNAs in human kidney and other tissues. Borden et al. (1995) also isolated human BGT1 cDNAs and reported that the human protein shares 91% and 87% sequence identity with canine and mouse BGT1, respectively. Heterologous expression of human BGT1 in mammalian cells conferred high–affinity GABA uptake.

[16161] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16162] Yamauchi, A.; Uchida, S.; Kwon, H. M.; Preston, A. S.; Robey, R. B.; Garcia-Perez, A.; Burg, M. B.; Handler, J. S. : Cloning of a Na(+) and Cl(-)-dependent betaine transporter that is regulated by hypertonicity. *J. Biol. Chem.* 267: 649-652, 1992. ; and

[16163] Rasola, A.; Galletta, L. J. V.; Barone, V.; Romeo, G.; Bagnasco, S. : Molecular cloning and functional characterization of a GABA/betaine transporter from human kidney. *FEBS Lett.* 373: 22.

[16164] Further studies establishing the function and utilities of SLC6A12 are found in John Hopkins OMIM database record ID 603080, and in cited publications numbered 1068-1070 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 18 (KOX 11) (ZNF18, Accession XM_085596) is another VGAM293 host target gene. ZNF18 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF18, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of ZNF18 BINDING SITE, designated SEQ ID:38250, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16165] Another function of VGAM293 is therefore inhibition of Zinc Finger Protein 18 (KOX 11) (ZNF18, Accession XM_085596). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF18. ABLIM (Accession NM_002313) is another VGAM293 host target gene. ABLIM BINDING SITE1 and ABLIM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABLIM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABLIM BINDING SITE1 and ABLIM BINDING SITE2, designated SEQ ID:8120 and SEQ ID:13553 respectively, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16166] Another function of VGAM293 is therefore inhibition of ABLIM (Accession NM_002313). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with ABLIM. ATPW (Accession NM_015684) is another VGAM293 host target gene. ATPW BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ATPW, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATPW BINDING SITE, designated SEQ ID:17909, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16167] Another function of VGAM293 is therefore inhibition of ATPW (Accession NM_015684). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATPW. KIAA1371 (Accession XM_114371) is another VGAM293 host target gene. KIAA1371 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1371, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1371 BINDING SITE, designated SEQ ID:42906, to the nucleotide sequence of

VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16168] Another function of VGAM293 is therefore inhibition of KIAA1371 (Accession XM_114371). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1371. KIAA1462 (Accession XM_166132) is another VGAM293 host target gene. KIAA1462 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1462, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1462 BINDING SITE, designated SEQ ID:43922, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16169] Another function of VGAM293 is therefore inhibition of KIAA1462 (Accession XM_166132). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1462. KIAA1643 (Accession XM_035371) is another VGAM293 host target gene. KIAA1643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by KIAA1643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1643 BINDING SITE, designated SEQ ID:32238, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16170] Another function of VGAM293 is therefore inhibition of KIAA1643 (Accession XM_035371). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1643. MGC13251 (Accession NM_032714) is another VGAM293 host target gene. MGC13251 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13251 BINDING SITE, designated SEQ ID:26437, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16171] Another function of VGAM293 is therefore inhibition of MGC13251 (Accession NM_032714). Accordingly, utilities

of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13251. MGC15476 (Accession NM_145056) is another VGAM293 host target gene. MGC15476 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC15476, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC15476 BINDING SITE, designated SEQ ID:29690, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16172] Another function of VGAM293 is therefore inhibition of MGC15476 (Accession NM_145056). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC15476. LOC114971 (Accession XM_054936) is another VGAM293 host target gene. LOC114971 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC114971, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC114971 BINDING SITE, designated SEQ ID:36210, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16173] Another function of VGAM293 is therefore inhibition of LOC114971 (Accession XM_054936). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC114971. LOC144848 (Accession XM_056770) is another VGAM293 host target gene. LOC144848 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144848, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144848 BINDING SITE, designated SEQ ID:36423, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16174] Another function of VGAM293 is therefore inhibition of LOC144848 (Accession XM_056770). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144848. LOC201181 (Accession XM_113916) is another VGAM293 host target gene. LOC201181 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC201181, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201181 BINDING SITE, designated SEQ ID:42534, to the nucleotide sequence of VGAM293 RNA, herein designated VGAM RNA, also designated SEQ ID:3004.

[16175] Another function of VGAM293 is therefore inhibition of LOC201181 (Accession XM_113916). Accordingly, utilities of VGAM293 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201181. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 294 (VGAM294) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16176] VGAM294 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM294 was detected is described hereinabove with reference to Figs. 1-8.

[16177] VGAM294 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16178] VGAM294 gene encodes a VGAM294 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM294 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM294 precursor RNA is designated SEQ ID:280, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:280 is located at position 77095 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16179] VGAM294 precursor RNA folds onto itself, forming VGAM294 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[16180] An enzyme complex designated DICER COMPLEX, `dices` the VGAM294 folded precursor RNA into VGAM294 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM294 RNA is designated SEQ ID:3005, and is provided hereinbelow with reference to the sequence listing part.

[16181] VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM294 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16182] VGAM294 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM294 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM294 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM294 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16183] The complementary binding of VGAM294 RNA, herein designated VGAM RNA, to host target binding sites on VGAM294 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM294 host target RNA into VGAM294 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16184] It is appreciated that VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM294 host target genes. The mRNA of each one of this plurality of VGAM294 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM294 RNA, herein designated VGAM RNA, and which when bound by VGAM294 RNA causes inhibition of translation of respective one or more VGAM294 host target proteins.

[16185] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM294 gene, herein designated VGAM GENE, on one or more VGAM294 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16186] It is yet further appreciated that a function of VGAM294 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM294 correlate with, and may be deduced from, the identity of the host target genes which VGAM294 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16187] Nucleotide sequences of the VGAM294 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM294 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM294 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM294 are further described hereinbelow with reference to Table 1.

[16188] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM294 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM294 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16189] As mentioned hereinabove with reference to Fig. 1, a function of VGAM294 gene, herein designated VGAM is inhibition of expression of VGAM294 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM294 correlate with, and may be deduced from, the identity of the target genes which VGAM294 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16190] Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962) is a VGAM294 host target gene. IL22RA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL22RA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2

illustrates the complementarity of the nucleotide sequences of IL22RA2 BINDING SITE, designated SEQ ID:27523, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16191] A function of VGAM294 is therefore inhibition of Interleukin 22 Receptor, Alpha 2 (IL22RA2, Accession NM_052962), a gene which induces the production of acute-phase reactants. Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL22RA2. The function of IL22RA2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167.Solute Carrier Family 1 (glial high affinity glutamate transporter), Member 3 (SLC1A3, Accession NM_004172) is another VGAM294 host target gene. SLC1A3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC1A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC1A3 BINDING SITE, designated SEQ

ID:10384, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16192] Another function of VGAM294 is therefore inhibition of Solute Carrier Family 1 (glial high affinity glutamate transporter), Member 3 (SLC1A3, Accession NM_004172), a gene which is a transporter molecule that regulates neurotransmitter concentrations at excitatory synapses of the mammalian CNS. Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC1A3. The function of SLC1A3 has been established by previous studies.

Kirschner et al. (1994) mapped the human EAAT1 gene to 5p13 by fluorescence in situ hybridization. They used interspecific backcross analysis to map the murine homolog to chromosome 15 in a region of homology to human 5p13. They commented that the EAAT1 locus may be related to the syndrome of microcephaly and mental retardation observed by Keppen et al. (1992) in association with interstitial deletion of distal band 5p13. In the retina, the glutamate transporter GLAST is expressed in Muller cells, whereas the glutamate transporter GLT1 is found only in cones and various types of bipolar cells. To inves-

tigate the functional role of this differential distribution of glutamate transporters, Harada et al. (1998) analyzed Glst and Glt1 mutant mice. In Glst-deficient mice, the electroretinogram b-wave and oscillatory potentials were reduced and retinal damage after ischemia was exacerbated, whereas Glt1-deficient mice showed almost normal electroretinograms and mildly increased retinal damage after ischemia. These results demonstrated that Glst is required for normal signal transmission between photoreceptors and bipolar cells and that both Glst and Glt1 play a neuroprotective role during ischemia in the retina.

[16193] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16194] Kirschner, M. A.; Arriza, J. L.; Copeland, N. G.; Gilbert, D. J.; Jenkins, N. A.; Magenis, E.; Amara, S. G. : The mouse and human excitatory amino acid transporter gene (EAAT1) maps to mouse chromosome 15 and a region of syntenic homology on human chromosome 5. *Genomics* 22: 631–633, 1994. ; and

[16195] Harada, T.; Harada, C.; Watanabe, M.; Inoue, Y.; Sakagawa, T.; Nakayama, N.; Sasaki, S.; Okuyama, S.; Watase, K.; Wada, K.; Tanaka, K. : Functions of the two glutamate

transporters GLAST a.

[16196] Further studies establishing the function and utilities of SLC1A3 are found in John Hopkins OMIM database record ID 600111, and in cited publications numbered 2918–2924 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ubiquitin–conjugating Enzyme E2A (RAD6 homolog) (UBE2A, Accession NM_003336) is another VGAM294 host target gene. UBE2A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UBE2A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UBE2A BINDING SITE, designated SEQ ID:9342, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16197] Another function of VGAM294 is therefore inhibition of Ubiquitin–conjugating Enzyme E2A (RAD6 homolog) (UBE2A, Accession NM_003336), a gene which catalyzes the covalent attachment of ubiquitin to other proteins and is required for postreplication repair of uv–damaged dna. Accordingly, utilities of VGAM294 include diagnosis, pre–

vention and treatment of diseases and clinical conditions associated with UBE2A. The function of UBE2A has been established by previous studies. As deduced from the pleiotropic phenotype of rad6 deletion mutants in *Saccharomyces cerevisiae*, the RAD6 protein plays an important role in various cellular processes. The protein is strongly conserved in eukaryotic evolution, a property that permitted Koken et al. (1991) to clone human homologs by evolutionary walking using *Schizosaccharomyces pombe* and *Drosophila melanogaster* homologs as 'intermediates.' The human HHR6A and HHR6B proteins (HHR for human homolog of rad6) shared about 95% amino acid sequence identity with each other and about 70% amino acid sequence with their yeast counterparts, but notably lacked the acidic C-terminal domain, the occurrence of which seemed to be limited to *S. cerevisiae* rad6. By in situ hybridization with biotinylated probes, Koken et al. (1992) localized the RAD6A gene to Xq24-q25 and the RAD6B gene (OMIM Ref. No. 179095) to 5q23-q31. The assignment of RAD6A to the X chromosome was confirmed with an X-specific human-mouse/hamster somatic cell hybrid panel. This gene is also symbolized UBE2A (for ubiquitin-conjugating enzyme E2A).

- [16198] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [16199] Koken, M. H. M.; Reynolds, P.; Jaspers–Dekker, I.; Prakash, L.; Prakash, S.; Bootsma, D.; Hoeijmakers, J. H. J. : Structural and functional conservation of two human homologs of the yeast DNA repair gene RAD6. Proc. Nat. Acad. Sci. 88: 8865–8869, 1991. ; and
- [16200] Koken, M. H. M.; Smit, E. M. E.; Jaspers–Dekker, I.; Oostra, B. A.; Hagemeyer, A.; Bootsma, D.; Hoeijmakers, J. H. J. : Localization of two human homologs, HHR6A and HHR6B, of the yeas.
- [16201] Further studies establishing the function and utilities of UBE2A are found in John Hopkins OMIM database record ID 312180, and in cited publications numbered 8412 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0193 (Accession NM_014766) is another VGAM294 host target gene. KIAA0193 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0193, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu–

cleotide sequences of KIAA0193 BINDING SITE, designated SEQ ID:16545, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16202] Another function of VGAM294 is therefore inhibition of KIAA0193 (Accession NM_014766). Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0193. KIAA0972 (Accession NM_014930) is another VGAM294 host target gene. KIAA0972 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0972, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0972 BINDING SITE, designated SEQ ID:17227, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16203] Another function of VGAM294 is therefore inhibition of KIAA0972 (Accession NM_014930). Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0972. LOC145231 (Accession XM_096740) is another

VGAM294 host target gene. LOC145231 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145231, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145231 BINDING SITE, designated SEQ ID:40520, to the nucleotide sequence of VGAM294 RNA, herein designated VGAM RNA, also designated SEQ ID:3005.

[16204] Another function of VGAM294 is therefore inhibition of LOC145231 (Accession XM_096740). Accordingly, utilities of VGAM294 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145231. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 295 (VGAM295) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16205] VGAM295 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM295 was detected is described

hereinabove with reference to Figs. 1–8.

[16206] VGAM295 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16207] VGAM295 gene encodes a VGAM295 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM295 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM295 precursor RNA is designated SEQ ID:281, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:281 is located at position 83820 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16208] VGAM295 precursor RNA folds onto itself, forming VGAM295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an

accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16209] An enzyme complex designated DICER COMPLEX, `dices` the VGAM295 folded precursor RNA into VGAM295 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 47%) nucleotide sequence of VGAM295 RNA is designated SEQ ID:3006, and is provided hereinbelow with reference to the sequence listing part.

[16210] VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM295 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16211] VGAM295 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites lo-

cated in untranslated regions of VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM295 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM295 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM295 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16212] The complementary binding of VGAM295 RNA, herein designated VGAM RNA, to host target binding sites on VGAM295 host target RNA, herein designated VGAM HOST

TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM295 host target RNA into VGAM295 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16213] It is appreciated that VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM295 host target genes. The mRNA of each one of this plurality of VGAM295 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM295 RNA, herein designated VGAM RNA, and which when bound by VGAM295 RNA causes inhibition of translation of respective one or more VGAM295 host target proteins.

[16214] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM295 gene, herein designated VGAM GENE, on one or more VGAM295 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a spe-

cific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16215] It is yet further appreciated that a function of VGAM295 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM295 correlate with, and may be deduced from, the identity of the host target genes which VGAM295 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16216] Nucleotide sequences of the VGAM295 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM295 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding

of VGAM295 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM295 are further described hereinbelow with reference to Table 1.

[16217] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM295 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM295 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16218] As mentioned hereinabove with reference to Fig. 1, a function of VGAM295 gene, herein designated VGAM is inhibition of expression of VGAM295 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM295 correlate with, and may be deduced from, the identity of the target genes which VGAM295 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16219] Adenylate Cyclase 7 (ADCY7, Accession NM_001114) is a VGAM295 host target gene. ADCY7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ADCY7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADCY7 BINDING SITE, designated SEQ ID:6779, to the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA, also designated SEQ ID:3006.

[16220] A function of VGAM295 is therefore inhibition of Adenylate Cyclase 7 (ADCY7, Accession NM_001114), a gene which this a membrane-bound, Ca^{2+} -inhibitable adenylyl cyclase. Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADCY7. The function of ADCY7 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM108. Junctophilin 2 (JPH2, Accession XM_170491) is another VGAM295 host target gene. JPH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by JPH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of JPH2 BINDING SITE, designated SEQ ID:45332, to the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA,

also designated SEQ ID:3006.

[16221] Another function of VGAM295 is therefore inhibition of Junctophilin 2 (JPH2, Accession XM_170491), a gene which mediates cross talk between cell surface and intracellular ion channels. Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with JPH2. The function of JPH2 has been established by previous studies. Junctional complexes between the plasma membrane (PM) and endoplasmic/sarcoplasmic reticulum (ER/SR) are a common feature of all excitable cell types and mediate cross talk between cell surface and intracellular ion channels. Takeshima et al. (2000) identified the junctophilins (JPs), a conserved family of proteins that are components of the junctional complexes. JPs are composed of a C-terminal hydrophobic segment spanning the ER/SR membrane and a remaining cytoplasmic domain that shows specific affinity for the PM. In mouse, there are at least 3 JP subtypes: Jp1, Jp2, and Jp3. By screening genomic DNA libraries, Nishi et al. (2000) isolated the human JP1 (OMIM Ref. No. 605266) and JP2 genes, and by screening a brain cDNA library, they isolated a cDNA encoding human JP3 (OMIM Ref. No. 605268). The JP2 gene encodes a deduced 696-amino

acid protein. The human JPs share an overall sequence identity of 39%, and they share characteristic structural features with their rabbit and mouse counterparts. RNA blot hybridization indicated that the tissue-specific expression patterns of the JP genes in human are essentially the same as those in mouse; JP1 was expressed as a 4.5-kb transcript in skeletal muscle and at low levels in heart, JP2 was expressed as a 4.1-kb transcript in heart and skeletal muscle, and JP3 was expressed as a 4.6-kb transcript in brain. The protein-coding sequence is interrupted by 4 introns in each JP gene. By FISH, Nishi et al. (2000) mapped the JP2 gene to 20q12 and determined that the JP genes do not cluster on the human genome. Takeshima et al. (2000) showed that Jp2 is abundantly expressed in mouse heart, and mutant mice lacking Jp2 exhibited embryonic lethality. Cardiac myocytes from the mutant mice showed deficiency of the junctional membrane complexes and abnormal calcium transients. These results suggested that JPs are important components of junctional membrane complexes.

[16222] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [16223] Nishi, M.; Mizushima, A.; Nakagawara, K.; Takeshima, H. : Characterization of human junctophilin subtype genes. Biochem. Biophys. Res. Commun. 273: 920–927, 2000. ; and
- [16224] Takeshima, H.; Komazaki, S.; Nishi, M.; Iino, M.; Kangawa, K. : Junctophilins: a novel family of junctional membrane complex proteins. Molec. Cell 6: 11–22, 2000.
- [16225] Further studies establishing the function and utilities of JPH2 are found in John Hopkins OMIM database record ID 605267, and in cited publications numbered 5036–5037 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP564O0423 (Accession XM_166254) is another VGAM295 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44061, to the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA, also designated SEQ ID:3006.
- [16226] Another function of VGAM295 is therefore inhibition of

DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. LOC124801 (Accession XM_058850) is another VGAM295 host target gene.

LOC124801 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124801, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124801 BINDING SITE, designated SEQ ID:36763, to the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA, also designated SEQ ID:3006.

[16227] Another function of VGAM295 is therefore inhibition of LOC124801 (Accession XM_058850). Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124801. LOC57086 (Accession NM_020351) is another VGAM295 host target gene. LOC57086 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC57086, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC57086 BINDING SITE, designated SEQ ID:21618, to the nucleotide sequence of VGAM295 RNA, herein designated VGAM RNA, also designated SEQ ID:3006.

[16228] Another function of VGAM295 is therefore inhibition of LOC57086 (Accession NM_020351). Accordingly, utilities of VGAM295 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57086. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 296 (VGAM296) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16229] VGAM296 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM296 was detected is described hereinabove with reference to Figs. 1–8.

[16230] VGAM296 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM296 host target gene, herein

designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16231] VGAM296 gene encodes a VGAM296 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM296 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM296 precursor RNA is designated SEQ ID:282, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:282 is located at position 80889 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[16232] VGAM296 precursor RNA folds onto itself, forming VGAM296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16233] An enzyme complex designated DICER COMPLEX, `dices` the VGAM296 folded precursor RNA into VGAM296 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 52%) nucleotide sequence of VGAM296 RNA is designated SEQ ID:3007, and is provided hereinbelow with reference to the sequence listing part.

[16234] VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM296 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16235] VGAM296 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM296 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM296 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16236] The complementary binding of VGAM296 RNA, herein designated VGAM RNA, to host target binding sites on VGAM296 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM296 host target RNA into VGAM296 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[16237] It is appreciated that VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM296 host target genes. The mRNA of each one of this plurality of VGAM296 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM296 RNA, herein designated VGAM RNA, and which when bound by VGAM296 RNA causes inhibition of translation of respective one or more VGAM296 host target proteins.

[16238] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM296 gene, herein designated VGAM GENE, on one or more VGAM296 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16239] It is yet further appreciated that a function of VGAM296 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM296 correlate with, and may be deduced from, the identity of the host target genes which VGAM296 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16240] Nucleotide sequences of the VGAM296 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM296 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM296 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM296 are further described hereinbelow with reference to Table 1.

[16241] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM296 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM296 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16242] As mentioned hereinabove with reference to Fig. 1, a function of VGAM296 gene, herein designated VGAM is inhibition of expression of VGAM296 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM296 correlate with, and may be deduced from, the identity of the target genes which VGAM296 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16243] Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719) is a VGAM296 host target gene. CACNA1C BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CACNA1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA1C BINDING SITE, designated SEQ ID:6378, to the nucleotide sequence of

VGAM296 RNA, herein designated VGAM RNA, also designated SEQ ID:3007.

[16244] A function of VGAM296 is therefore inhibition of Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719), a gene which is alpha-1 subunit of DHP-sensitive calcium channels from cardiac muscle and the brain. Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA1C. The function of CACNA1C and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM182. Ubiquitin Specific Protease 6 (Tre-2 onco-gene) (USP6, Accession XM_165948) is another VGAM296 host target gene. USP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP6 BINDING SITE, designated SEQ ID:43806, to the nucleotide sequence of VGAM296 RNA, herein designated VGAM RNA, also designated SEQ ID:3007.

[16245] Another function of VGAM296 is therefore inhibition of Ubiquitin Specific Protease 6 (Tre-2 oncogene) (USP6, Accession XM_165948), a gene which has an atp-independent isopeptidase activity, cleaving at the carboxyl terminus of the ubiquitin moiety. Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP6. The function of USP6 has been established by previous studies. The TRE locus was first isolated from NIH 3T3 cells transfected with human Ewing sarcoma DNA (Nakamura et al., 1988). Huebner et al. (1988) found that the locus is discontinuous in human cells and is composed of 3 major genetic elements originating 5-prime to 3-prime from human chromosomes 5, 18, and 17. Nakamura et al. (1992) cloned transcripts from the chromosome 17 portion of TRE from a cDNA library of cytoplasmic poly(A) RNA from TRE-transfected NIH 3T3 tumor cells. They obtained a novel cDNA, the 5-prime part of which overlapped the TRE transcript, and named its locus of origin TRE2. The complete cDNA spans 8,201 bp and possesses an unusually long noncoding region and a translatable region with 2 open reading frames (ORF). In one cDNA clone, the presence of 2 insertion sequences suggested

the possibility of alternative splicing. Transfection-tumorigenicity assays with the ORFs subcloned into expression vectors were positive for the ORF adjacent to the 5-prime noncoding region and negative for the second, downstream ORF. Analysis of the 786-amino acid sequence deduced from the 5-prime ORF predicted a highly hydrophilic protein with 2 charge clusters suggesting nucleic acid-binding properties. When used as a probe, the cloned sequence detected RNA transcripts in a wide variety of human cancer cells regardless of their lineage of origin from different tissues, but not in human cells from normal tissue. By chromosomal in situ hybridization, Nakamura et al. (1992) mapped the TRE2 gene to 17q11.

[16246] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16247] Huebner, K.; Cannizzaro, L. A.; Nakamura, T.; Hillova, J.; Mariage-Samson, R.; Hecht, F.; Hill, M.; Croce, C. M. : A rearranged transforming gene, tre, is made up of human sequences derived from chromosome regions 5q, 17q and 18q. *Oncogene* 3: 449-455, 1988. ; and

[16248] Nakamura, T.; Hillova, J.; Mariage-Samson, R.; Onno, M.; Huebner, K.; Cannizzaro, L. A.; Boghosian-Sell, L.; Croce,

C. M.; Hill, M. : A novel transcriptional unit of the tre oncogene wid.

[16249] Further studies establishing the function and utilities of USP6 are found in John Hopkins OMIM database record ID 604334, and in cited publications numbered 4987–4989 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Olfactomedin 3 (OLFM3, Accession XM_088951) is another VGAM296 host target gene. OLFM3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OLFM3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OLFM3 BINDING SITE, designated SEQ ID:39957, to the nucleotide sequence of VGAM296 RNA, herein designated VGAM RNA, also designated SEQ ID:3007.

[16250] Another function of VGAM296 is therefore inhibition of Olfactomedin 3 (OLFM3, Accession XM_088951). Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OLFM3. LOC256714 (Accession XM_172798) is another VGAM296 host target gene. LOC256714 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256714 BINDING SITE, designated SEQ ID:46081, to the nucleotide sequence of VGAM296 RNA, herein designated VGAM RNA, also designated SEQ ID:3007.

[16251] Another function of VGAM296 is therefore inhibition of LOC256714 (Accession XM_172798). Accordingly, utilities of VGAM296 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256714. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 297 (VGAM297) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16252] VGAM297 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM297 was detected is described hereinabove with reference to Figs. 1-8.

[16253] VGAM297 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16254] VGAM297 gene encodes a VGAM297 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM297 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM297 precursor RNA is designated SEQ ID:283, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:283 is located at position 88463 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16255] VGAM297 precursor RNA folds onto itself, forming VGAM297 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[16256] An enzyme complex designated DICER COMPLEX, `dices` the VGAM297 folded precursor RNA into VGAM297 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM297 RNA is designated SEQ ID:3008, and is provided hereinbelow with reference to the sequence listing part.

[16257] VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM297 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16258] VGAM297 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM297 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM297 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM297 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16259] The complementary binding of VGAM297 RNA, herein designated VGAM RNA, to host target binding sites on VGAM297 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM297 host target RNA into VGAM297 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16260] It is appreciated that VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM297 host target genes. The mRNA of each one of this plurality of VGAM297 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM297 RNA, herein designated VGAM RNA, and which when bound by VGAM297 RNA causes inhibition of translation of respective one or more VGAM297 host target proteins.

[16261] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM297 gene, herein designated VGAM GENE, on one or more VGAM297 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16262] It is yet further appreciated that a function of VGAM297 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM297 correlate with, and may be deduced from, the identity of the host target genes which VGAM297 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16263] Nucleotide sequences of the VGAM297 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM297 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM297 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM297 are further described hereinbelow with reference to Table 1.

[16264] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM297 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM297 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16265] As mentioned hereinabove with reference to Fig. 1, a function of VGAM297 gene, herein designated VGAM is inhibition of expression of VGAM297 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM297 correlate with, and may be deduced from, the identity of the target genes which VGAM297 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16266] Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM_003899) is a VGAM297 host target gene. ARHGEF7 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ARHGEF7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF7 BINDING SITE, designated SEQ ID:9984, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16267] A function of VGAM297 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 7 (ARHGEF7, Accession NM_003899), a gene which acts as a rac1 guanine nucleotide exchange factor (gef) and can induce membrane ruffling. Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF7. The function of ARHGEF7 has been established by previous studies. p21 (CDKN1A; 116899)–activated kinases, or PAKs (e.g., PAK1; 602590), bind to and are activated by Rho family GTPases, such as CDC42 (OMIM Ref. No. 116952) and RAC (see OMIM Ref. No. RAC1; 602048). PAKs are implicated in the regulation of gene expression, cytoskeletal architecture, and apoptosis. By screening rat tissue extracts for binding to PAK1, peptide microsequencing, and primer walking, Manser et al. (1998) isolated a rat cDNA encoding Pixb. Pixb is approximately 97% identical to the human cDNA KIAA0142 identified by Nagase et al. (1995). By

screening a mouse thymus expression cDNA library, Oh et al. (1997) isolated a cDNA encoding p85SPR (85-kD, SH3 domain-containing, proline-rich protein), which is 93% identical to KIAA0142, or human PIXB. Using a yeast 2-hybrid screen with PAK3 (OMIM Ref. No. 300142) as bait, Bagrodia et al. (1998) also isolated PIXB, which they called COOL1, from a HeLa cell cDNA library. Sequence analysis predicted that the 646-amino acid PIXB protein contains an N-terminal SH3 domain, a Dbl-homology (DH) domain, a pleckstrin homology (PH) domain, 2 putative nuclear localization signals, 2 leucine zipper motifs, and a proline-rich region. Northern blot analysis by Manser et al. (1998) revealed ubiquitous expression of an approximately 4.4-kb transcript. By immunofluorescence microscopy, they showed that the SH3 domain of PIXB is required for recruitment of PAK1 to CDC42-driven focal complexes. Their functional analysis demonstrated that PIXB acts as a RAC1 guanine nucleotide exchange factor (GEF) and can induce membrane ruffling.

[16268] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16269] Bagrodia, S.; Taylor, S. J.; Jordon, K. A.; Van Aelst, L.; Ceri-

one, R. A. : A novel regulator of p21-activated kinases. J. Biol. Chem. 273: 23633-23636, 1998. ; and

[16270] Manser, E.; Loo, T.-H.; Koh, C.-G.; Zhao, Z.-S.; Chen, X.-Q.; Tan, L.; Tan, I.; Leung, T.; Lim, L. : PAK kinases are directly coupled to the PIX family of nucleotide exchange factors. M.

[16271] Further studies establishing the function and utilities of ARHGEF7 are found in John Hopkins OMIM database record ID 605477, and in cited publications numbered 6977, 1081 and 10969 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Colony Stimulating Factor 1 Receptor, Formerly McDonough Feline Sarcoma Viral (v-fms) Oncogene Homolog (CSF1R, Accession NM_005211) is another VGAM297 host target gene. CSF1R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CSF1R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CSF1R BINDING SITE, designated SEQ ID:11710, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16272] Another function of VGAM297 is therefore inhibition of Colony Stimulating Factor 1 Receptor, Formerly McDonough Feline Sarcoma Viral (v-fms) Oncogene Homolog (CSF1R, Accession NM_005211), a gene which is involved in regulation of growth and differentiation of myeloid cells. Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CSF1R. The function of CSF1R has been established by previous studies. The FMS oncogene was assigned to chromosome 5 by study of mouse-human somatic cell hybrids. The location was narrowed to 5q34 by the study of hamster-human cell hybrids with well-defined deletions of 5q (Groffen et al., 1984). The order on the long arm was found to be centromere--leuS--HEXB--EMTB--CFMS--CHR. By in situ hybridization, Le Beau et al. (1986) assigned FMS to 5q33 and GM-CSF (OMIM Ref. No. 138960) to 5q23-q31. Both genes were deleted in the 5q- chromosome from bone marrow cells of 2 patients with refractory anemia and del(5)(q15q33.3). From study of other cases they concluded that FMS is located in band 5q33.2 or 5q33.3 rather than 5q34-q35 as reported earlier. The FMS oncogene is the same as the receptor for colony-stimulating

factor-1, otherwise known as macrophage colony-stimulating factor (OMIM Ref. No. 120420). Kondo et al. (2000) showed that a clonogenic common lymphoid progenitor, a bone marrow-resident cell that gives rise exclusively to lymphocytes (T, B, and natural killer cells), can be redirected to the myeloid lineage by stimulation through exogenously expressed interleukin-2 receptor (OMIM Ref. No. 146710) and GM-CSF receptor (138981, 306250). Analysis of mutants of the beta-chain of the IL2 receptor revealed that the granulocyte and monocyte differentiation signals are triggered by different cytoplasmic domains, showing that the signaling pathways responsible for these unique developmental outcomes are separable. Finally, Kondo et al. (2000) showed that the endogenous myelomonocytic cytokine receptors for GM-CSF and macrophage colony-stimulating factor (CSF1R) are expressed at low to moderate levels on the more primitive hematopoietic stem cells, are absent on common lymphoid progenitors, and are upregulated after myeloid lineage induction by IL2 (OMIM Ref. No. 147680). Kondo et al. (2000) concluded that cytokine signaling can regulate cell fate decisions and proposed that a critical step in lymphoid commitment is downregulation of cytokine re-

ceptors that drive myeloid cell development

- [16273] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [16274] Le Beau, M. M.; Westbrook, C. A.; Diaz, M. O.; Larson, R. A.; Rowley, J. D.; Gasson, J. C.; Golde, D. W.; Sherr, C. J. : Evidence for the involvement of GM-CSF and FMS in the deletion (5q) in myeloid disorders. *Science* 231: 984–987, 1986. ; and
- [16275] Kondo, M.; Scherer, D. C.; Miyamoto, T.; King, A. G.; Akashi, K.; Sugamura, K.; Weissman, I. L. : Cell-fate conversion of lymphoid-committed progenitors by instructive actions of cytokine.
- [16276] Further studies establishing the function and utilities of CSF1R are found in John Hopkins OMIM database record ID 164770, and in cited publications numbered 5100–510 and 3818–3826 listed in the bibliography section herein–below, which are also hereby incorporated by reference. RAB27A, Member RAS Oncogene Family (RAB27A, Accession NM_004580) is another VGAM297 host target gene. RAB27A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB27A, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB27A BINDING SITE, designated SEQ ID:10929, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16277] Another function of VGAM297 is therefore inhibition of RAB27A, Member RAS Oncogene Family (RAB27A, Accession NM_004580). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB27A. Transmembrane, Prostate Androgen Induced RNA (TMEPAI, Accession NM_020182) is another VGAM297 host target gene. TMEPAI BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TMEPAI, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TMEPAI BINDING SITE, designated SEQ ID:21406, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16278] Another function of VGAM297 is therefore inhibition of

Transmembrane, Prostate Androgen Induced RNA

(TMEPAI, Accession NM_020182). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TMEPAI.

KIAA0367 (Accession XM_041018) is another VGAM297 host target gene. KIAA0367 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0367, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0367 BINDING SITE, designated SEQ ID:33424, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16279] Another function of VGAM297 is therefore inhibition of KIAA0367 (Accession XM_041018). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0367. KIAA0543 (Accession XM_044213) is another VGAM297 host target gene. KIAA0543 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0543, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0543 BINDING SITE, designated SEQ ID:34177, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16280] Another function of VGAM297 is therefore inhibition of KIAA0543 (Accession XM_044213). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0543. KIAA0794 (Accession XM_087353) is another VGAM297 host target gene. KIAA0794 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0794, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0794 BINDING SITE, designated SEQ ID:39179, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16281] Another function of VGAM297 is therefore inhibition of KIAA0794 (Accession XM_087353). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA0794. KIAA1486 (Accession XM_041126) is another VGAM297 host target gene. KIAA1486 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1486, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1486 BINDING SITE, designated SEQ ID:33462, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16282] Another function of VGAM297 is therefore inhibition of KIAA1486 (Accession XM_041126). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1486. Small EDRK-rich Factor 2 (SERF2, Accession NM_005770) is another VGAM297 host target gene. SERF2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SERF2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERF2 BINDING SITE, designated SEQ ID:12342, to the nucleotide sequence of VGAM297 RNA, herein designated

VGAM RNA, also designated SEQ ID:3008.

[16283] Another function of VGAM297 is therefore inhibition of Small EDRK-rich Factor 2 (SERF2, Accession NM_005770). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERF2. LOC158987 (Accession XM_099015) is another VGAM297 host target gene. LOC158987 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158987, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158987 BINDING SITE, designated SEQ ID:42047, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16284] Another function of VGAM297 is therefore inhibition of LOC158987 (Accession XM_099015). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158987. LOC165352 (Accession XM_103974) is another VGAM297 host target gene. LOC165352 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC165352, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC165352 BINDING SITE, designated SEQ ID:42157, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16285] Another function of VGAM297 is therefore inhibition of LOC165352 (Accession XM_103974). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC165352. LOC219649 (Accession XM_167562) is another VGAM297 host target gene. LOC219649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC219649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC219649 BINDING SITE, designated SEQ ID:44666, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16286] Another function of VGAM297 is therefore inhibition of LOC219649 (Accession XM_167562). Accordingly, utilities

of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC219649. LOC221692 (Accession XM_166420) is another VGAM297 host target gene. LOC221692 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC221692, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221692 BINDING SITE, designated SEQ ID:44299, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16287] Another function of VGAM297 is therefore inhibition of LOC221692 (Accession XM_166420). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221692. LOC90826 (Accession XM_034321) is another VGAM297 host target gene. LOC90826 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC90826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC90826 BINDING SITE, designated SEQ ID:32048, to the nucleotide sequence of VGAM297 RNA, herein designated VGAM RNA, also designated SEQ ID:3008.

[16288] Another function of VGAM297 is therefore inhibition of LOC90826 (Accession XM_034321). Accordingly, utilities of VGAM297 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90826. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 298 (VGAM298) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16289] VGAM298 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM298 was detected is described hereinabove with reference to Figs. 1–8.

[16290] VGAM298 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16291] VGAM298 gene encodes a VGAM298 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM298 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM298 precursor RNA is designated SEQ ID:284, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:284 is located at position 29595 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[16292] VGAM298 precursor RNA folds onto itself, forming VGAM298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16293] An enzyme complex designated DICER COMPLEX, `dices` the VGAM298 folded precursor RNA into VGAM298 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM298 RNA is designated SEQ ID:3009, and is provided hereinbelow with reference to the sequence listing part.

[16294] VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM298 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16295] VGAM298 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM298 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM298 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[16296] The complementary binding of VGAM298 RNA, herein designated VGAM RNA, to host target binding sites on VGAM298 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM298 host target RNA into VGAM298 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16297] It is appreciated that VGAM298 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM298 host target genes. The mRNA of each one of this plurality of VGAM298 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM298 RNA, herein designated VGAM RNA, and which when bound by VGAM298 RNA causes inhibition of translation of respective one or more VGAM298 host target proteins.

[16298] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM298 gene, herein designated VGAM GENE, on one or more VGAM298 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[16299] It is yet further appreciated that a function of VGAM298 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM298 correlate with, and may be deduced from, the identity of the host target genes which VGAM298 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16300] Nucleotide sequences of the VGAM298 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM298 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM298 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM298 are further described hereinbelow with reference to Table 1.

[16301] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM298 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM298 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16302] As mentioned hereinabove with reference to Fig. 1, a function of VGAM298 gene, herein designated VGAM is inhibition of expression of VGAM298 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM298 correlate with, and may be deduced from, the identity of the target genes which VGAM298 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16303] CD3Z Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Accession NM_000734) is a VGAM298 host target gene. CD3Z BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD3Z, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD3Z BINDING SITE, designated SEQ ID:6390, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16304] A function of VGAM298 is therefore inhibition of CD3Z

Antigen, Zeta Polypeptide (TiT3 complex) (CD3Z, Accession NM_000734), a gene which may involve in assembly and expression of the tcr complex as well as signal transduction upon antigen triggering. Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD3Z. The function of CD3Z and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM167.

Cytoplasmic Linker Associated Protein 1 (CLASP1, Accession XM_037105) is another VGAM298 host target gene. CLASP1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CLASP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLASP1 BINDING SITE, designated SEQ ID:32544, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16305] Another function of VGAM298 is therefore inhibition of Cytoplasmic Linker Associated Protein 1 (CLASP1, Accession XM_037105), a gene which plays a role in the local

regulation of microtubule dynamics . Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLASP1. The function of CLASP1 has been established by previous studies. CLIP170 (OMIM Ref. No. 179838) and CLIP115 (OMIM Ref. No. 603432) are cytoplasmic linker proteins that associate specifically with the ends of growing microtubules and may act as anticatastrophe factors. Using a yeast 2-hybrid screen with an N-terminal region of CLIP115 as bait, followed by cDNA library screening, RACE analysis, and EST database searching, Akhmanova et al. (2001) identified mouse and human cDNAs encoding 2 CLIP-associated proteins, CLASP1 and CLASP2 (OMIM Ref. No. 605853). The CLASPs are homologous to a *Drosophila* microtubule-associated protein termed Orbit or Mast. CLASP1 is identical to the protein encoded by a partial cDNA, KIAA0622, identified by Ishikawa et al. (1998), although the KIAA0622 protein lacks the N-terminal 249 amino acids of the 1,538-amino acid CLASP1 protein reported by Akhmanova et al. (2001). CLASP2 shares approximately 75% identity with the KIAA0627 protein, which is encoded by a partial cDNA also identified by Ishikawa et al. (1998). There are several CLASP isoforms

due to alternative splicing. Northern blot analysis of mouse tissues detected highest expression of Clasp1 in brain, heart, and testis, while Clasp2 mRNAs were enriched in the brain. The Clasp2-beta transcript appeared to be brain specific. By RT-PCR analysis, Ishikawa et al. (1998) detected ubiquitous expression of CLASP1, which they called KIAA0622. Akhmanova et al. (2001) showed that CLASPs bind CLIPs and microtubules, colocalize with the CLIPs at microtubule distal ends, and have microtubule-stabilizing effects in transfected cells. After serum induction, CLASPs relocate to distal segments of microtubules at the leading edge of motile fibroblasts. Akhmanova et al. (2001) provided evidence that this asymmetric CLASP distribution is mediated by phosphatidylinositol 3-kinase (see OMIM Ref. No. 171834) and glycogen synthase kinase 3-beta (OMIM Ref. No. 605004). Antibody injections suggested that CLASP2 is required for the orientation of stabilized microtubules toward the leading edge. The authors proposed that CLASPs are involved in the local regulation of microtubule dynamics in response to positional cues.

[16306] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

[16307] Akhmanova, A.; Hoogenraad, C. C.; Drabek, K.; Stepanova, T.; Dortland, B.; Verkerk, T.; Vermeulen, W.; Burgering, B. M.; De Zeeuw, C. I.; Grosveld, F.; Galjart, N. : CLASPs are CLIP-115 and -170 associating proteins involved in the regional regulation of microtubule dynamics in motile fibroblasts. Cell 104: 923-935, 2001. ; and

[16308] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete sequ.

[16309] Further studies establishing the function and utilities of CLASP1 are found in John Hopkins OMIM database record ID 605852, and in cited publications numbered 662 and 9440 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Diacylglycerol O-acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM_032564) is another VGAM298 host target gene. DGAT2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DGAT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide

sequences of DGAT2 BINDING SITE, designated SEQ ID:26291, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16310] Another function of VGAM298 is therefore inhibition of Diacylglycerol O-acyltransferase Homolog 2 (mouse) (DGAT2, Accession NM_032564). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DGAT2. Dmx-like 1 (DMXL1, Accession NM_005509) is another VGAM298 host target gene. DMXL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DMXL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DMXL1 BINDING SITE, designated SEQ ID:12025, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16311] Another function of VGAM298 is therefore inhibition of Dmx-like 1 (DMXL1, Accession NM_005509). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DMXL1. Sorting Nexin 9 (SNX9, Accession NM_016224) is another VGAM298 host target gene. SNX9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNX9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNX9 BINDING SITE, designated SEQ ID:18327, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16312] Another function of VGAM298 is therefore inhibition of Sorting Nexin 9 (SNX9, Accession NM_016224). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNX9. Unc-5 Homolog B (C. elegans) (UNC5C, Accession NM_003728) is another VGAM298 host target gene. UNC5C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by UNC5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UNC5C BINDING SITE, designated SEQ ID:9818, to the nucleotide sequence of VGAM298 RNA,

herein designated VGAM RNA, also designated SEQ ID:3009.

[16313] Another function of VGAM298 is therefore inhibition of Unc-5 Homolog B (*C. elegans*) (UNC5C, Accession NM_003728), a gene which is a putative receptor for netrin, which is involved in axon guidance. Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UNC5C. The function of UNC5C has been established by previous studies. Migration of neurons from proliferative zones to their functional sites is fundamental to the normal development of the central nervous system. Mice homozygous for the rostral cerebellar malformation (*rcm*) mutation exhibit cerebellar and midbrain defects, apparently as a result of abnormal neuronal migration. Ackerman et al. (1997) reported that in *rcm*-mutant mice, the cerebellum is smaller and has fewer folia than in wildtype, ectopic cerebellar cells are present in midbrain regions by 3 days after birth, and there are abnormalities in postnatal cerebellar-neuronal migration. The authors isolated cDNAs encoding the *rcm* protein (*Rcm*). Sequence analysis revealed that the predicted 931-amino acid mouse protein is a transmembrane protein that contains 2 im-

munoglobulin (Ig)-like domains and 2 type I thrombospondin (THBS1; 188060) motifs in the extracellular region. Ig and THBS1 domains are also found in the extracellular region of the *C. elegans* UNC5 transmembrane protein, and the C-terminal 865-amino acid region of Rcm is 30% identical to UNC5. Ackerman et al. (1997) stated that the UNC5 protein is essential for dorsal guidance of pioneer axons and for the movement of cells away from the netrin ligand. In the developing brain of vertebrates, netrin-1 (OMIM Ref. No. 601614) plays a role in both cell migration and axonal guidance. Leonardo et al. (1997) demonstrated that Rcm binds netrin-1 in vitro. Ackerman et al. (1997) concluded that Rcm and its ligand are important in critical migratory and/or cell-proliferation events during cerebellar development. Przyborski et al. (1998) found that disruption of the mouse rcm gene, also called the Unc5h3 gene, resulted in a failure of tangentially migrating granule cells to recognize the rostral boundary of the cerebellum. By searching an EST database for sequences related to the Unc5h3 gene, Ackerman and Knowles (1998) identified a partial human fetal brain cDNA encoding UNC5C, the human Unc5h3 homolog. Using 5-prime RACE, they cloned a cDNA corre-

sponding to the entire UNC5C coding region. The predicted 931-amino acid human protein has the overall domain structure of UNC5 family proteins, and is 97% identical to Unc5h3. Northern blot analysis revealed that the 9.5-kb UNC5 mRNA is expressed in brain and heart, and at low levels in kidney.

[16314] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16315] Przyborski, S. A.; Knowles, B. B.; Ackerman, S. L. : Embryonic phenotype of Unc5h3 mutant mice suggests chemorepulsion during the formation of the rostral cerebellar boundary. *Development* 125: 41–50, 1998. ; and

[16316] Ackerman, S. L.; Knowles, B. B. : Cloning and mapping of the UNC5C gene to human chromosome 4q21–q23. *Genomics* 52: 205–208, 1998.

[16317] Further studies establishing the function and utilities of UNC5C are found in John Hopkins OMIM database record ID 603610, and in cited publications numbered 2885–2889 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. UV Radiation Resistance Associated Gene (UVRAG, Accession NM_003369) is another VGAM298 host target gene.

UVRAG BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by UVRAG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of UVRAG BINDING SITE, designated SEQ ID:9396, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16318] Another function of VGAM298 is therefore inhibition of UV Radiation Resistance Associated Gene (UVRAG, Accession NM_003369). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with UVRAG. FLJ10097 (Accession XM_043653) is another VGAM298 host target gene. FLJ10097 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10097, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10097 BINDING SITE, designated SEQ ID:33990, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ

ID:3009.

[16319] Another function of VGAM298 is therefore inhibition of FLJ10097 (Accession XM_043653). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10097. FLJ23416 (Accession NM_032238) is another VGAM298 host target gene. FLJ23416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23416 BINDING SITE, designated SEQ ID:25959, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16320] Another function of VGAM298 is therefore inhibition of FLJ23416 (Accession NM_032238). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23416. KIAA1317 (Accession XM_098368) is another VGAM298 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA1317, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41620, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16321] Another function of VGAM298 is therefore inhibition of KIAA1317 (Accession XM_098368). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. NYD-SP29 (Accession XM_059085) is another VGAM298 host target gene. NYD-SP29 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NYD-SP29, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NYD-SP29 BINDING SITE, designated SEQ ID:36861, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16322] Another function of VGAM298 is therefore inhibition of NYD-SP29 (Accession XM_059085). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NYD-SP29. SSH2 (Accession XM_030846) is another VGAM298 host target gene. SSH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SSH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SSH2 BINDING SITE, designated SEQ ID:31175, to the nucleotide sequence of VGAM298 RNA, herein designated VGAM RNA, also designated SEQ ID:3009.

[16323] Another function of VGAM298 is therefore inhibition of SSH2 (Accession XM_030846). Accordingly, utilities of VGAM298 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SSH2. Fig.

1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 299 (VGAM299) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16324] VGAM299 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM299 was detected is described hereinabove with reference to Figs. 1–8.

[16325] VGAM299 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16326] VGAM299 gene encodes a VGAM299 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM299 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM299 precursor RNA is designated SEQ ID:285, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:285 is

located at position 59096 relative to the genome of Epi-
phyas Postvittana Nucleopolyhedrovirus.

[16327] VGAM299 precursor RNA folds onto itself, forming VGAM299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16328] An enzyme complex designated DICER COMPLEX, `dices` the VGAM299 folded precursor RNA into VGAM299 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM299 RNA is designated SEQ ID:3010, and is provided hereinbelow with reference to the sequence listing part.

[16329] VGAM299 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM299 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16330] VGAM299 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM299 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM299 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM299 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[16331] The complementary binding of VGAM299 RNA, herein designated VGAM RNA, to host target binding sites on VGAM299 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM299 host target RNA into VGAM299 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16332] It is appreciated that VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM299 host target genes. The mRNA of each one of this plurality of VGAM299 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM299 RNA, herein designated VGAM RNA, and which when bound by VGAM299 RNA causes inhibition of translation of respective one or more VGAM299

host target proteins.

[16333] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM299 gene, herein designated VGAM GENE, on one or more VGAM299 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16334] It is yet further appreciated that a function of VGAM299 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucle-

opolyhedrovirus. Specific functions, and accordingly utilities, of VGAM299 correlate with, and may be deduced from, the identity of the host target genes which VGAM299 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16335] Nucleotide sequences of the VGAM299 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM299 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM299 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM299 are further described hereinbelow with reference to Table 1.

[16336] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM299 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM299 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16337] As mentioned hereinabove with reference to Fig. 1, a function of VGAM299 gene, herein designated VGAM is inhibition of expression of VGAM299 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM299 correlate with, and may be deduced from, the identity of the target genes which VGAM299 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16338] Apolipoprotein L, 1 (APOL1, Accession NM_003661) is a VGAM299 host target gene. APOL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL1 BINDING SITE, designated SEQ ID:9735, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16339] A function of VGAM299 is therefore inhibition of Apolipoprotein L, 1 (APOL1, Accession NM_003661), a gene which may participate in reverse cholesterol transport from peripheral cells to the liver. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with APOL1. The function of APOL1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference

to VGAM235.ATP Synthase, H⁺ Transporting, Mitochondrial F1 Complex, Beta Polypeptide (ATP5B, Accession XM_006710) is another VGAM299 host target gene. ATP5B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ATP5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP5B BINDING SITE, designated SEQ ID:30007, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16340] Another function of VGAM299 is therefore inhibition of ATP Synthase, H⁺ Transporting, Mitochondrial F1 Complex, Beta Polypeptide (ATP5B, Accession XM_006710). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP5B. CAAX Box 1 (CXX1, Accession NM_003928) is another VGAM299 host target gene. CXX1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CXX1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

CXX1 BINDING SITE, designated SEQ ID:10026, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16341] Another function of VGAM299 is therefore inhibition of CAAX Box 1 (CXX1, Accession NM_003928). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CXX1. 5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870) is another VGAM299 host target gene. HTR4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTR4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR4 BINDING SITE, designated SEQ ID:6543, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16342] Another function of VGAM299 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 4 (HTR4, Accession NM_000870), a gene which mediates calcium channel currents. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with HTR4. The function of HTR4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM65. Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558) is another VGAM299 host target gene. PPP1R8 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PPP1R8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP1R8 BINDING SITE, designated SEQ ID:28859, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16343] Another function of VGAM299 is therefore inhibition of Protein Phosphatase 1, Regulatory (inhibitor) Subunit 8 (PPP1R8, Accession NM_138558), a gene which is an inhibitor subunit of the major nuclear protein phosphatase-1 (pp-1). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP1R8. The function of PPP1R8 and its association with various diseases and clin-

ical conditions, has been established by previous studies, as described hereinabove with reference to VGAM101. Transcription Factor 19 (SC1) (TCF19, Accession XM_175167) is another VGAM299 host target gene. TCF19 BINDING SITE1 and TCF19 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by TCF19, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCF19 BINDING SITE1 and TCF19 BINDING SITE2, designated SEQ ID:46657 and SEQ ID:46706 respectively, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16344] Another function of VGAM299 is therefore inhibition of Transcription Factor 19 (SC1) (TCF19, Accession XM_175167), a gene which plays an important role in the transcription of genes required for the later stages of cell cycle progression. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF19. The function of TCF19 has been established by previous studies. Ku et al. (1991) cloned a growth-regulated cDNA by differential

screening of a mouse 3T3 cell line library to identify transcripts induced by serum stimulation. Transcripts of the gene, designated SC1, were detectable beginning at about 8 hours after stimulation. The mouse cDNA was used to clone the human SC1 cDNA. The 2.6-kb cDNA encoded a deduced 359-amino acid polypeptide with features characteristic of transactivating factors. The gene was mapped by in situ hybridization to chromosome 6p21-p22. The bacterially expressed protein had the predicted size of 39 kD. Krishnan et al. (1995) mapped TCF19 with POU5F1 (OMIM Ref. No. 164177) to a 0.2-Mb region between HLAC (OMIM Ref. No. 142840) and the so-called S gene (OMIM Ref. No. 602593) at 6p21.3. POU5F1 and TCF19 are about 130 kb telomeric of HLAC and about 600 bp from each other.

[16345] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16346] Krishnan, B. R.; Jamry, I.; Chaplin, D. D. : Feature mapping of the HLA class I region: localization of the POU5F1 and TCF19 genes. *Genomics* 30: 53-58, 1995. ; and

[16347] Ku, D.-H.; Chang, C.; Koniecki, J.; Cannizzaro, L. A.; Boghosian-Sell, L.; Alder, H.; Baserga, R. : A new growth-

regulated complementary DNA with the sequence of a putative trans-activ.

[16348] Further studies establishing the function and utilities of TCF19 are found in John Hopkins OMIM database record ID 600912, and in cited publications numbered 9610–9611 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Tumor Necrosis Factor (ligand) Superfamily, Member 5 (hyper-IgM syndrome) (TNFSF5, Accession NM_000074) is another VGAM299 host target gene. TNFSF5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TNFSF5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TNFSF5 BINDING SITE, designated SEQ ID:5520, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16349] Another function of VGAM299 is therefore inhibition of Tumor Necrosis Factor (ligand) Superfamily, Member 5 (hyper-IgM syndrome) (TNFSF5, Accession NM_000074). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with TNFSF5. Williams–Beuren Syndrome Chromosome Region 1 (WBSCR1, Accession NM_022170) is another VGAM299 host target gene. WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WBSCR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WBSCR1 BINDING SITE1 and WBSCR1 BINDING SITE2, designated SEQ ID:22726 and SEQ ID:25709 respectively, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16350] Another function of VGAM299 is therefore inhibition of Williams–Beuren Syndrome Chromosome Region 1 (WBSCR1, Accession NM_022170), a gene which stimulates protein translation. Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WBSCR1. The function of WBSCR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM110.

Chromosome 7 Open Reading Frame 13

(C7orf13, Accession NM_032625) is another VGAM299 host target gene. C7orf13 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by C7orf13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C7orf13 BINDING SITE, designated SEQ ID:26341, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16351] Another function of VGAM299 is therefore inhibition of Chromosome 7 Open Reading Frame 13 (C7orf13, Accession NM_032625). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C7orf13. Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM_006549) is another VGAM299 host target gene. CAMKK2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CAMKK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CAMKK2 BINDING SITE,

designated SEQ ID:13313, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16352] Another function of VGAM299 is therefore inhibition of Calcium/calmodulin-dependent Protein Kinase Kinase 2, Beta (CAMKK2, Accession NM_006549). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CAMKK2. DKFZP434K1772 (Accession XM_041936) is another VGAM299 host target gene. DKFZP434K1772 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP434K1772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434K1772 BINDING SITE, designated SEQ ID:33635, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16353] Another function of VGAM299 is therefore inhibition of DKFZP434K1772 (Accession XM_041936). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated

with DKFZP434K1772. FLJ11850 (Accession NM_022741) is another VGAM299 host target gene. FLJ11850 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ11850, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11850 BINDING SITE, designated SEQ ID:22952, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16354] Another function of VGAM299 is therefore inhibition of FLJ11850 (Accession NM_022741). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11850. FLJ12934 (Accession NM_022899) is another VGAM299 host target gene. FLJ12934 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12934, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12934 BINDING SITE, designated SEQ ID:23179, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3010.

[16355] Another function of VGAM299 is therefore inhibition of FLJ12934 (Accession NM_022899). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12934. FLJ22795 (Accession NM_025084) is another VGAM299 host target gene. FLJ22795 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22795, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22795 BINDING SITE, designated SEQ ID:24691, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16356] Another function of VGAM299 is therefore inhibition of FLJ22795 (Accession NM_025084). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22795. Interleukin 14 (IL14, Accession XM_170924) is another VGAM299 host target gene. IL14 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by IL14, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL14 BINDING SITE, designated SEQ ID:45705, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16357] Another function of VGAM299 is therefore inhibition of Interleukin 14 (IL14, Accession XM_170924). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL14. KIAA0161 (Accession NM_014746) is another VGAM299 host target gene. KIAA0161 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0161, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0161 BINDING SITE, designated SEQ ID:16434, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16358] Another function of VGAM299 is therefore inhibition of KIAA0161 (Accession NM_014746). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0161. KIAA0240 (Accession XM_166479) is another VGAM299 host target gene. KIAA0240 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0240, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0240 BINDING SITE, designated SEQ ID:44408, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16359] Another function of VGAM299 is therefore inhibition of KIAA0240 (Accession XM_166479). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0240. KIAA1340 (Accession XM_044836) is another VGAM299 host target gene. KIAA1340 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1340, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1340 BINDING SITE, designated SEQ ID:34300, to the

nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16360] Another function of VGAM299 is therefore inhibition of KIAA1340 (Accession XM_044836). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1340. KIAA1872 (Accession XM_031917) is another VGAM299 host target gene. KIAA1872 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1872, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1872 BINDING SITE, designated SEQ ID:31521, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16361] Another function of VGAM299 is therefore inhibition of KIAA1872 (Accession XM_031917). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1872. MGC4170 (Accession NM_024312) is another VGAM299 host target gene. MGC4170 BINDING SITE is HOST TARGET binding site found in the 5' untranslated

region of mRNA encoded by MGC4170, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4170 BINDING SITE, designated SEQ ID:23606, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16362] Another function of VGAM299 is therefore inhibition of MGC4170 (Accession NM_024312). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4170. Ring Finger Protein 40 (RNF40, Accession NM_014771) is another VGAM299 host target gene. RNF40 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RNF40, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RNF40 BINDING SITE, designated SEQ ID:16569, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16363] Another function of VGAM299 is therefore inhibition of

Ring Finger Protein 40 (RNF40, Accession NM_014771). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RNF40. Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863) is another VGAM299 host target gene. SPTLC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SPTLC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SPTLC2 BINDING SITE, designated SEQ ID:11287, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16364] Another function of VGAM299 is therefore inhibition of Serine Palmitoyltransferase, Long Chain Base Subunit 2 (SPTLC2, Accession NM_004863). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SPTLC2. Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession XM_053740) is another VGAM299 host target gene. TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2 are HOST TARGET binding sites found in untrans-

lated regions of mRNA encoded by TP53INP1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TP53INP1 BINDING SITE1 and TP53INP1 BINDING SITE2, designated SEQ ID:36121 and SEQ ID:27112 respectively, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16365] Another function of VGAM299 is therefore inhibition of Tumor Protein P53 Inducible Nuclear Protein 1 (TP53INP1, Accession XM_053740). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TP53INP1.

LOC145717 (Accession XM_039771) is another VGAM299 host target gene. LOC145717 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145717, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145717 BINDING SITE, designated SEQ ID:33193, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16366] Another function of VGAM299 is therefore inhibition of LOC145717 (Accession XM_039771). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145717. LOC146488 (Accession XM_047748) is another VGAM299 host target gene. LOC146488 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146488, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146488 BINDING SITE, designated SEQ ID:35041, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16367] Another function of VGAM299 is therefore inhibition of LOC146488 (Accession XM_047748). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146488. LOC148089 (Accession XM_086040) is another VGAM299 host target gene. LOC148089 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148089, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148089 BINDING SITE, designated SEQ ID:38453, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16368] Another function of VGAM299 is therefore inhibition of LOC148089 (Accession XM_086040). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148089. LOC200772 (Accession XM_117275) is another VGAM299 host target gene. LOC200772 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200772, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200772 BINDING SITE, designated SEQ ID:43347, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16369] Another function of VGAM299 is therefore inhibition of LOC200772 (Accession XM_117275). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC200772. LOC220537 (Accession XM_165406) is another VGAM299 host target gene. LOC220537 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC220537, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220537 BINDING SITE, designated SEQ ID:43624, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16370] Another function of VGAM299 is therefore inhibition of LOC220537 (Accession XM_165406). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220537. LOC221882 (Accession XM_166507) is another VGAM299 host target gene. LOC221882 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC221882, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221882 BINDING SITE, designated SEQ ID:44435, to the nucleotide sequence of VGAM299 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3010.

[16371] Another function of VGAM299 is therefore inhibition of LOC221882 (Accession XM_166507). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221882. LOC253675 (Accession XM_172990) is another VGAM299 host target gene. LOC253675 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253675, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253675 BINDING SITE, designated SEQ ID:46266, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16372] Another function of VGAM299 is therefore inhibition of LOC253675 (Accession XM_172990). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253675. LOC54466 (Accession NM_019003) is another VGAM299 host target gene. LOC54466 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC54466, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC54466 BINDING SITE, designated SEQ ID:21076, to the nucleotide sequence of VGAM299 RNA, herein designated VGAM RNA, also designated SEQ ID:3010.

[16373] Another function of VGAM299 is therefore inhibition of LOC54466 (Accession NM_019003). Accordingly, utilities of VGAM299 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC54466. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 300 (VGAM300) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16374] VGAM300 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM300 was detected is described hereinabove with reference to Figs. 1–8.

[16375] VGAM300 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana

Nucleopolyhedrovirus. VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16376] VGAM300 gene encodes a VGAM300 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM300 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM300 precursor RNA is designated SEQ ID:286, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:286 is located at position 99030 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16377] VGAM300 precursor RNA folds onto itself, forming VGAM300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16378] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM300 folded precursor RNA into VGAM300 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM300 RNA is designated SEQ ID:3011, and is provided hereinbelow with reference to the sequence listing part.

[16379] VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM300 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16380] VGAM300 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM300 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM300 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16381] The complementary binding of VGAM300 RNA, herein designated VGAM RNA, to host target binding sites on VGAM300 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM300 host target RNA into VGAM300 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16382] It is appreciated that VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM300 host target genes. The mRNA of each one of this plurality of VGAM300 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM300 RNA, herein designated VGAM RNA, and which when bound by VGAM300 RNA causes inhibition of translation of respective one or more VGAM300 host target proteins.

[16383] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM300 gene, herein designated VGAM GENE, on one or more VGAM300 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16384] It is yet further appreciated that a function of VGAM300 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM300 correlate with, and may be deduced from, the identity of the host target genes which VGAM300 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16385] Nucleotide sequences of the VGAM300 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM300 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM300 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM300 are further described hereinbelow with reference to Table 1.

- [16386] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM300 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM300 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [16387] As mentioned hereinabove with reference to Fig. 1, a function of VGAM300 gene, herein designated VGAM is inhibition of expression of VGAM300 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM300 correlate with, and may be deduced from, the identity of the target genes which VGAM300 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [16388] Excision Repair Cross-complementing Rodent Repair Deficiency, Complementation Group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome)) (ERCC5, Accession NM_000123) is a VGAM300 host target gene. ERCC5 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ERCC5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of ERCC5 BINDING SITE, designated SEQ ID:5596, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16389] A function of VGAM300 is therefore inhibition of Excision Repair Cross-complementing Rodent Repair Deficiency, Complementation Group 5 (xeroderma pigmentosum, complementation group G (Cockayne syndrome)) (ERCC5, Accession NM_000123), a gene which single-stranded dna endonuclease involved in dna excision repair. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ERCC5. The function of ERCC5 has been established by previous studies. Hori et al. (1983) found that human chromosome 13 is involved in excision repair of UV-induced DNA damage. This was shown by studying somatic cell hybrids between a UV-sensitive mutant mouse cell line and normal human lymphocytes. The mouse line used had a defect that fell into complementation group I (of OMIM Ref. No. 278700). Siciliano (1987) found that UV-135 is the same as ERCM2; complementation of the two cell lines was not observed. Furthermore, ERCM2 is

the same as ERCC5. Previously, 2 patients with a rare combined xeroderma pigmentosum/Cockayne syndrome phenotype were identified: one within XP complementation group B (OMIM Ref. No. 133540) and one within complementation group D (OMIM Ref. No. 126340). Vermeulen et al. (1993) reported genetic studies of 2 unrelated, severely affected patients with clinical characteristics of Cockayne syndrome but with a biochemical defect typical of xeroderma pigmentosum. By complementation analysis, using somatic cell fusion and nuclear microinjection of cloned repair genes, they assigned these 2 patients to XP complementation group G. Volker et al. (2001) described the assembly of the NER complex in normal and repair-deficient (xeroderma pigmentosum) human cells by employing a novel technique of local ultraviolet irradiation combined with fluorescent antibody labeling. The damage-recognition complex XPC (OMIM Ref. No. 278720)–HR23B (OMIM Ref. No. 600062) appeared to be essential for the recruitment of all subsequent NER factors in the preincision complex, including transcription repair factor TFIIH. The authors found that XPA associates relatively late, is required for anchoring of ERCC1–XPF, and may be essential for activation of the endonuclease activ-

ity of XPG. These findings identified XPC as the earliest known NER factor in the reaction mechanism, gave insight into the order of subsequent NER components, provided evidence for a dual role of XPA, and supported a concept of sequential assembly of repair proteins at the site of damage rather than a preassembled repairosome.

[16390] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16391] Hori, T.; Shiomi, T.; Sato, K. : Human chromosome 13 compensates a DNA repair defect in UV-sensitive mouse cells by mouse-human cell hybridization. Proc. Nat. Acad. Sci. 80: 5655-5659, 1983. ; and

[16392] Volker, M.; Mone, M. J.; Karmakar, P.; van Hoffen, A.; Schul, W.; Vermeulen, W.; Hoeijmakers, J. H. J.; van Driel, R.; van Zeeland, A. A.; Mullenders, L. H. F. : Sequential assembly of.

[16393] Further studies establishing the function and utilities of ERCC5 are found in John Hopkins OMIM database record ID 133530, and in cited publications numbered 3101, 11354-11355, 3102, 11356-11369, 11369-11373, 1875-1876, 3690, 369 and 3671-1880 listed in the bibliography section hereinbelow, which are also hereby incor-

porated by reference. Interleukin 8 Receptor, Alpha (IL8RA, Accession NM_000634) is another VGAM300 host target gene. IL8RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL8RA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL8RA BINDING SITE, designated SEQ ID:6268, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16394] Another function of VGAM300 is therefore inhibition of Interleukin 8 Receptor, Alpha (IL8RA, Accession NM_000634), a gene which is the receptor to interleukin-8, which is a powerful neutrophils chemotactic factor. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL8RA. The function of IL8RA has been established by previous studies. Interleukin-8 (IL8; 146930) is a member of a family of pro-inflammatory cytokines. The best-characterized activities of IL8 include the chemoattraction and activation of neutrophils. Holmes et al. (1991) isolated a cDNA encoding an IL8 receptor from human neutrophils. The deduced amino acid sequence

showed that the receptor is a member of the superfamily of receptors that couple to guanine nucleotide binding proteins (G proteins). The sequence is 29% identical to that of receptors for the other neutrophil chemoattractants, fMet-Leu-Phe and C5a. Morris et al. (1992) mapped the type 1 interleukin-8 receptor gene to 2q35; see type 2 interleukin-8 receptor (OMIM Ref. No. 146928) for further information on the two IL8R genes. Mollereau et al. (1993) assigned the high-affinity receptor gene to the same region by in situ hybridization. Lloyd et al. (1993) assigned both the IL8RA and the IL8RB gene to chromosome 2 by polymerase chain reaction amplification and by Southern analysis of a panel of human/rodent somatic cell hybrid DNAs. The IL8R genes were further localized by in situ hybridization to 2q35. Palter et al. (2001) characterized the IL8 system, which includes IL8, its receptors IL8RA and IL8RB, and its degradative enzyme aminopeptidase N (OMIM Ref. No. 151530), in the human fallopian tube by immunohistochemistry. IL8 was found in the human fallopian tube predominantly in the epithelial cells and was present in greater amounts in the distal compared with the proximal tube. IL8RA and IL8RB localized in the tube in similar patterns. Aminopeptidase N was found in tubal

stromal tissue at the epithelial–stromal border and perivascularly. The authors concluded that the IL8 system may be an active component of tubal physiology and that aminopeptidase N may limit the systemic effects of epithelial IL8.

[16395] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16396] Morris, S. W.; Nelson, N.; Valentine, M. B.; Shapiro, D. N.; Look, A. T.; Kozlosky, C. J.; Beckmann, M. P.; Cerretti, D. P. : Assignment of the genes encoding human interleukin–8 receptor types 1 and 2 and an interleukin–8 receptor pseudogene to chromosome 2q35. *Genomics* 14: 685–691, 1992. ; and

[16397] Palter, S. F.; Mulayim, N.; Senturk, L.; Arici, A. : Interleukin–8 in the human fallopian tube. *J. Clin. Endocr. Metab.* 86: 2660–2667, 2001.

[16398] Further studies establishing the function and utilities of IL8RA are found in John Hopkins OMIM database record ID 146929, and in cited publications numbered 391 and 295–297 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Laminin, Alpha 4 (LAMA4, Accession NM_002290) is another

VGAM300 host target gene. LAMA4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LAMA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAMA4 BINDING SITE, designated SEQ ID:8071, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16399] Another function of VGAM300 is therefore inhibition of Laminin, Alpha 4 (LAMA4, Accession NM_002290), a gene which mediates the attachment, migration and organization of cells into tissues. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAMA4. The function of LAMA4 has been established by previous studies. Laminin, a multidomain glycoprotein, is the major noncollagenous constituent of basement membranes. It is composed of 3 nonidentical chains: A (OMIM Ref. No. 150320), B1 (OMIM Ref. No. 150240), and B2 (OMIM Ref. No. 150290). The laminins form a cruciform structure consisting of 3 short arms, each of which is formed from different chains, and a long arm composed of all 3 chains.

By screening a human keratinocyte cDNA library for type VII collagen sequences, Richards et al. (1994) isolated a new laminin alpha chain variant gene, LAMA4 (formerly called LAMA3). Northern blot analysis indicated that a cDNA encoding LAMA4 hybridized to a 6.45-kb mRNA, significantly smaller than the 9.5- to 10-kb mRNA of laminin A (Haaparanta et al., 1991). Using PCR on genomic DNA, flow-sorted chromosomes, and fluorescence in situ hybridization, Richards et al. (1994) localized the LAMA4 gene to human chromosome 6q21. In this abstract, the authors referred to the gene as LAMA3; in the related article, Richards et al. (1994) used the corrected symbol, LAMA4. Iivanainen et al. (1995) cloned the laminin alpha-4 cDNA by screening a fetal lung library with a PCR product generated from primers based on a partial laminin-like sequence reported by GenBank. The complete cDNA is approximately 6.2 kb long and encodes a predicted protein of 1,816 amino acids. The domain structure of the protein is similar to the alpha-3 chain (LAMA3, also called BM600), both of which resemble truncated versions of alpha-1 and alpha-2 in which approximately 1,200 residues at the amino end have been lost. Northern blots showed strong expression of the mRNA in

adult heart, lung, ovary, small and large intestines, liver, and placenta.

[16400] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16401] Iivanainen, A.; Sainio, K.; Sariola, H.; Tryggvason, K. : Primary structure and expression of a novel human laminin alpha-4 chain. FEBS Lett. 365: 183-188, 1995. ; and

[16402] Richards, A. J.; Al-Imara, L.; Carter, N. P.; Lloyd, J. C.; Leversha, M. A.; Pope, F. M. : Localization of the gene (LAMA4) to chromosome 6q21 and isolation of a partial cDNA encoding a.

[16403] Further studies establishing the function and utilities of LAMA4 are found in John Hopkins OMIM database record ID 600133, and in cited publications numbered 4368-1586 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prothymosin, Alpha (gene sequence 28) (PTMA, Accession NM_002823) is another VGAM300 host target gene. PTMA BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PTMA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Ta-

ble 2 illustrates the complementarity of the nucleotide sequences of PTMA BINDING SITE, designated SEQ ID:8693, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16404] Another function of VGAM300 is therefore inhibition of Prothymosin, Alpha (gene sequence 28) (PTMA, Accession NM_002823), a gene which may mediate immune function by conferring resistance to certain opportunistic infections. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTMA. The function of PTMA has been established by previous studies. The thymus gland produces several hormones or hormone-like substances which are derived from a polypeptide precursor containing (in the rat) 113 amino acids and known as prothymosin-alpha. A peptide containing 28 amino acid residues, named thymosin-alpha-1, was originally isolated from calf thymosin fraction 5 and shown to restore various aspects of immune function in several in vitro and in vivo test systems. Thymosin-alpha-1 was subsequently isolated from a similar fraction from human thymosin and reported to have the same amino acid sequence as bovine thymosin-alpha-1. Haritos et al. (1984) isolated from fresh rat thymus

a larger polypeptide named prothymosin- α , which contains the thymosin- α -1 sequence at its NH₂ terminus. Prothymosin- α has also been isolated from human thymus. Goodall et al. (1986) constructed a cDNA library from human spleen mRNA and screened for clones containing cDNAs coding for prothymosin- α . Eschenfeldt and Berger (1986) identified cDNA clones for human prothymosin- α in cDNA libraries from staphylococcal endotoxin A-stimulated normal human lymphocytes. The encoded protein was found to be highly acidic (54 residues out of 111) and shared over 90% sequence homology with rat prothymosin- α . The peptide hormone thymosin- α -1 appeared at positions 2-29 of the prothymosin- α amino acid sequence. Manrow et al. (1992) concluded that of the 6 members of the prothymosin- α gene family that have been cloned and sequenced, only one is functional. Szabo et al. (1993) isolated a genomic clone encoding PTMA and subcloned and sequenced the 5-prime regulatory region. They used the 5-prime flanking cloned probe to localize the prothymosin gene to human chromosome 2 by Southern analysis of somatic cell hybrids.

[16405] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [16406] Haritos, A. A.; Goodall, G. J.; Horecker, B. L. : Prothymosin alpha: isolation and properties of the major immunoreactive form of thymosin alpha-1 in rat thymus. Proc. Nat. Acad. Sci. 81: 1008-1011, 1984. ; and
- [16407] Manrow, R. E.; Leone, A.; Krug, M. S.; Eschenfeldt, W. H.; Berger, S. L. : The human prothymosin alpha gene family contains several processed pseudogenes lacking deleterious lesions. Ge.
- [16408] Further studies establishing the function and utilities of PTMA are found in John Hopkins OMIM database record ID 188390, and in cited publications numbered 5697-5701 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030668) is another VGAM300 host target gene. PTPRO BINDING SITE1 through PTPRO BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PTPRO, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPRO BINDING SITE1

through PTPRO BINDING SITE3, designated SEQ ID:25011, SEQ ID:25020 and SEQ ID:25030 respectively, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16409] Another function of VGAM300 is therefore inhibition of Protein Tyrosine Phosphatase, Receptor Type, O (PTPRO, Accession NM_030668), a gene which may function as a cell contact receptor that mediates and controls cell-cell signals. Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPRO. The function of PTPRO and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140.C1q and Tumor Necrosis Factor Related Protein 4 (C1QTNF4, Accession NM_031909) is another VGAM300 host target gene. C1QTNF4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C1QTNF4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C1QTNF4 BINDING SITE, designated SEQ ID:25654, to the nucleotide sequence of VGAM300

RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16410] Another function of VGAM300 is therefore inhibition of C1q and Tumor Necrosis Factor Related Protein 4 (C1QTNF4, Accession NM_031909). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C1QTNF4. Cell Division Cycle Associated 4 (CDCA4, Accession NM_017955) is another VGAM300 host target gene. CDCA4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CDCA4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDCA4 BINDING SITE, designated SEQ ID:19663, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16411] Another function of VGAM300 is therefore inhibition of Cell Division Cycle Associated 4 (CDCA4, Accession NM_017955). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDCA4. KIAA0876

(Accession XM_035625) is another VGAM300 host target gene. KIAA0876 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by KIAA0876, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0876 BINDING SITE, designated SEQ ID:32296, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16412] Another function of VGAM300 is therefore inhibition of KIAA0876 (Accession XM_035625). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0876. KIAA1257 (Accession XM_031577) is another VGAM300 host target gene. KIAA1257 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1257, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1257 BINDING SITE, designated SEQ ID:31433, to the nucleotide sequence of VGAM300 RNA, herein designated

VGAM RNA, also designated SEQ ID:3011.

[16413] Another function of VGAM300 is therefore inhibition of KIAA1257 (Accession XM_031577). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1257. Kelch-like 6 (Drosophila) (KLHL6, Accession NM_130446) is another VGAM300 host target gene. KLHL6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KLHL6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KLHL6 BINDING SITE, designated SEQ ID:28210, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16414] Another function of VGAM300 is therefore inhibition of Kelch-like 6 (Drosophila) (KLHL6, Accession NM_130446). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KLHL6. MAD4 (Accession NM_006454) is another VGAM300 host target gene. MAD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by MAD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAD4 BINDING SITE, designated SEQ ID:13172, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16415] Another function of VGAM300 is therefore inhibition of MAD4 (Accession NM_006454). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAD4. MGC13007 (Accession NM_032320) is another VGAM300 host target gene. MGC13007 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13007 BINDING SITE, designated SEQ ID:26121, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16416] Another function of VGAM300 is therefore inhibition of MGC13007 (Accession NM_032320). Accordingly, utilities

of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13007. MGC13251 (Accession NM_032714) is another VGAM300 host target gene. MGC13251 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC13251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13251 BINDING SITE, designated SEQ ID:26435, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16417] Another function of VGAM300 is therefore inhibition of MGC13251 (Accession NM_032714). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13251. Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971) is another VGAM300 host target gene. MRPL20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MRPL20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of MRPL20 BINDING SITE, designated SEQ ID:19700, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16418] Another function of VGAM300 is therefore inhibition of Mitochondrial Ribosomal Protein L20 (MRPL20, Accession NM_017971). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MRPL20. PHACS (Accession NM_032592) is another VGAM300 host target gene. PHACS BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PHACS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PHACS BINDING SITE, designated SEQ ID:26324, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16419] Another function of VGAM300 is therefore inhibition of PHACS (Accession NM_032592). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PHACS.

Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531) is another VGAM300 host target gene. PRKWNK2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by PRKWNK2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRKWNK2 BINDING SITE, designated SEQ ID:43521, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16420] Another function of VGAM300 is therefore inhibition of Protein Kinase, Lysine Deficient 2 (PRKWNK2, Accession XM_117531). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRKWNK2. SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession NM_003003) is another VGAM300 host target gene. SEC14L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SEC14L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC14L1

BINDING SITE, designated SEQ ID:8906, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16421] Another function of VGAM300 is therefore inhibition of SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession NM_003003). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC14L1. SEC8 (Accession NM_021807) is another VGAM300 host target gene. SEC8 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC8, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC8 BINDING SITE, designated SEQ ID:22361, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16422] Another function of VGAM300 is therefore inhibition of SEC8 (Accession NM_021807). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC8. Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353) is another VGAM300 host target gene. ZD-

HHC2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by ZDHHC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC2 BINDING SITE, designated SEQ ID:18487, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16423] Another function of VGAM300 is therefore inhibition of Zinc Finger, DHHC Domain Containing 2 (ZDHHC2, Accession NM_016353). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZDHHC2. LOC145123 (Accession XM_041473) is another VGAM300 host target gene. LOC145123 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC145123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145123 BINDING SITE, designated SEQ ID:33534, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3011.

[16424] Another function of VGAM300 is therefore inhibition of LOC145123 (Accession XM_041473). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145123. LOC147229 (Accession XM_085742) is another VGAM300 host target gene. LOC147229 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC147229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147229 BINDING SITE, designated SEQ ID:38316, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16425] Another function of VGAM300 is therefore inhibition of LOC147229 (Accession XM_085742). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147229. LOC151009 (Accession XM_097992) is another VGAM300 host target gene. LOC151009 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC151009, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151009 BINDING SITE, designated SEQ ID:41291, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16426] Another function of VGAM300 is therefore inhibition of LOC151009 (Accession XM_097992). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151009. LOC220058 (Accession XM_166258) is another VGAM300 host target gene. LOC220058 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC220058, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220058 BINDING SITE, designated SEQ ID:44083, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16427] Another function of VGAM300 is therefore inhibition of LOC220058 (Accession XM_166258). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC220058. LOC254892 (Accession XM_170951) is another VGAM300 host target gene. LOC254892 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254892, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254892 BINDING SITE, designated SEQ ID:45737, to the nucleotide sequence of VGAM300 RNA, herein designated VGAM RNA, also designated SEQ ID:3011.

[16428] Another function of VGAM300 is therefore inhibition of LOC254892 (Accession XM_170951). Accordingly, utilities of VGAM300 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254892. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 301 (VGAM301) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16429] VGAM301 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM301 was detected is described hereinabove with reference to Figs. 1–8.

[16430] VGAM301 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16431] VGAM301 gene encodes a VGAM301 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM301 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM301 precursor RNA is designated SEQ ID:287, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:287 is located at position 49379 relative to the genome of Epiphyas Postvittana Nucleopolyhedrovirus.

[16432] VGAM301 precursor RNA folds onto itself, forming VGAM301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16433] An enzyme complex designated DICER COMPLEX, `dices` the VGAM301 folded precursor RNA into VGAM301 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM301 RNA is designated SEQ ID:3012, and is provided hereinbelow with reference to the sequence listing part.

[16434] VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM301 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16435] VGAM301 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM301 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM301 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16436] The complementary binding of VGAM301 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM301 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM301 host target RNA into VGAM301 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16437] It is appreciated that VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM301 host target genes. The mRNA of each one of this plurality of VGAM301 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM301 RNA, herein designated VGAM RNA, and which when bound by VGAM301 RNA causes inhibition of translation of respective one or more VGAM301 host target proteins.

[16438] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM301 gene, herein designated VGAM GENE, on one or more VGAM301 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16439] It is yet further appreciated that a function of VGAM301 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM301 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM301 correlate with, and may be deduced from, the identity of the host target genes which VGAM301 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16440] Nucleotide sequences of the VGAM301 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

5' duced 5' VGAM301 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM301 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM301 are further described hereinbelow with reference to Table 1.

[16441] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM301 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM301 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16442] As mentioned hereinabove with reference to Fig. 1, a function of VGAM301 gene, herein designated VGAM is inhibition of expression of VGAM301 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM301 correlate with, and may be deduced from, the identity of the target genes which VGAM301 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16443] FLJ14686 (Accession NM_032825) is a VGAM301 host target gene. FLJ14686 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by FLJ14686, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14686 BINDING SITE, designated SEQ ID:26599, to the nucleotide sequence of VGAM301 RNA, herein designated VGAM RNA, also designated SEQ ID:3012.

[16444] A function of VGAM301 is therefore inhibition of FLJ14686 (Accession NM_032825). Accordingly, utilities of VGAM301 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14686. HTMP10 (Accession NM_033207) is another VGAM301 host target gene. HTMP10 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HTMP10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTMP10 BINDING SITE, designated SEQ ID:27050, to the nucleotide sequence of VGAM301 RNA, herein designated VGAM RNA, also designated SEQ ID:3012.

[16445] Another function of VGAM301 is therefore inhibition of HTMP10 (Accession NM_033207). Accordingly, utilities of

VGAM301 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTMP10. SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession NM_003003) is another VGAM301 host target gene. SEC14L1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEC14L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEC14L1 BINDING SITE, designated SEQ ID:8900, to the nucleotide sequence of VGAM301 RNA, herein designated VGAM RNA, also designated SEQ ID:3012.

[16446] Another function of VGAM301 is therefore inhibition of SEC14-like 1 (*S. cerevisiae*) (SEC14L1, Accession NM_003003). Accordingly, utilities of VGAM301 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEC14L1. LOC153688 (Accession XM_098416) is another VGAM301 host target gene. LOC153688 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153688, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING

SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153688 BINDING SITE, designated SEQ ID:41654, to the nucleotide sequence of VGAM301 RNA, herein designated VGAM RNA, also designated SEQ ID:3012.

[16447] Another function of VGAM301 is therefore inhibition of LOC153688 (Accession XM_098416). Accordingly, utilities of VGAM301 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153688. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 302 (VGAM302) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16448] VGAM302 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM302 was detected is described hereinabove with reference to Figs. 1-8.

[16449] VGAM302 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM302 host target gene, herein

designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16450] VGAM302 gene encodes a VGAM302 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM302 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM302 precursor RNA is designated SEQ ID:288, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:288 is located at position 66246 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[16451] VGAM302 precursor RNA folds onto itself, forming VGAM302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16452] An enzyme complex designated DICER COMPLEX, `dices` the VGAM302 folded precursor RNA into VGAM302 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM302 RNA is designated SEQ ID:3013, and is provided hereinbelow with reference to the sequence listing part.

[16453] VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM302 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16454] VGAM302 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM302 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM302 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16455] The complementary binding of VGAM302 RNA, herein designated VGAM RNA, to host target binding sites on VGAM302 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM302 host target RNA into VGAM302 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[16456] It is appreciated that VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM302 host target genes. The mRNA of each one of this plurality of VGAM302 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM302 RNA, herein designated VGAM RNA, and which when bound by VGAM302 RNA causes inhibition of translation of respective one or more VGAM302 host target proteins.

[16457] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM302 gene, herein designated VGAM GENE, on one or more VGAM302 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16458] It is yet further appreciated that a function of VGAM302 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM302 correlate with, and may be deduced from, the identity of the host target genes which VGAM302 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16459] Nucleotide sequences of the VGAM302 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM302 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM302 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM302 are further described hereinbelow with reference to Table 1.

[16460] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM302 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM302 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16461] As mentioned hereinabove with reference to Fig. 1, a function of VGAM302 gene, herein designated VGAM is inhibition of expression of VGAM302 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM302 correlate with, and may be deduced from, the identity of the target genes which VGAM302 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16462] Cholinergic Receptor, Muscarinic 1 (CHRM1, Accession XM_170669) is a VGAM302 host target gene. CHRM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CHRM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHRM1 BINDING SITE, designated SEQ ID:45443, to the nucleotide sequence of VGAM302 RNA, herein designated

VGAM RNA, also designated SEQ ID:3013.

[16463] A function of VGAM302 is therefore inhibition of Cholinergic Receptor, Muscarinic 1 (CHRM1, Accession XM_170669), a gene which mediates various cellular responses. Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHRM1. The function of CHRM1 has been established by previous studies. Goyal (1989) stated that 5 distinct but related muscarinic receptors had been identified, with apparent molecular weights ranging from 51,452 to 66,127. These glycosylated proteins have single chains of 460 to 590 amino acids that are thought to span the plasma membrane 7 times, creating 4 extracellular domains, 7 helical hydrophobic transmembrane domains, and 4 intracellular domains. Each protein is the product of a different gene without introns in the coding sequence, and the amino acid sequences in the receptor subtypes are remarkably homologous among different animal species (Bonner et al., 1987; Peralta et al., 1987; Bonner et al., 1988; Liao et al., 1989). The nomenclature is confusing (Eglen and Whiting, 1986; Goyal, 1989). In structure and evolution, muscarinic receptors are quite distinct from their pharmacologic kin, the nico-

tinic receptors (see OMIM Ref. No. 100690, 100710, 100720, 100730). By means of analysis of somatic cell hybrids and by both isotopic and nonisotopic in situ hybridization, Bonner et al. (1991) assigned the CHRM1 gene to 11q12-q13. Courseaux et al. (1996) used a combination of methods to refine maps of the approximately 5-Mb region of 11q13 that includes MEN1 (OMIM Ref. No. 131100). They proposed the following gene order: cen-

PGA-

FTH1--UGB--AHNAK--ROM1--MDU1--CHRM1--COX8--
EMK1--FKBP2--PLCB3--[PYGM,
ZFM1]--FAU--CAPN1--[MLK3,
RELA]--FOSL1--SEA--CFL1--tel.

[16464] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16465] Bonner, T. I.; Buckley, N. J.; Young, A. C.; Brann, M. R. : Identification of a family of muscarinic acetylcholine receptor genes. Science 237: 527-532, 1987. ; and

[16466] Bonner, T. I.; Modi, W. S.; Seuanez, H. N.; O'Brien, S. J. : Chromosomal mapping of five human genes encoding

muscarinic acetylcholine receptors. (Abstract) Cytogenet. Cell Genet. 58: 1.

[16467] Further studies establishing the function and utilities of CHRM1 are found in John Hopkins OMIM database record ID 118510, and in cited publications numbered 1269 and 3984–3658 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dishevelled Associated Activator of Morphogenesis 1 (DAAM1, Accession NM_014992) is another VGAM302 host target gene. DAAM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM1 BINDING SITE, designated SEQ ID:17366, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16468] Another function of VGAM302 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 1 (DAAM1, Accession NM_014992), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM302 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with DAAM1. The function of DAAM1 has been established by previous studies. By screening size-fractionated brain cDNA libraries for cDNAs with the potential to encode proteins larger than 50 kD, Ishikawa et al. (1998) identified a cDNA which they designated KIAA0666. KIAA0666 encodes a 1,085-amino acid protein predicted to function in cell division. It is 68% identical to the KIAA0381 protein (DAAM2; 606627). RT-PCR analysis detected expression of KIAA0666 in all tissues tested. Wnt (see OMIM Ref. No. 164975) signaling via the frizzled receptor (Fz; OMIM Ref. No. 600667) controls cell polarity and movement during development. Habas et al. (2001) reported that in human cells and during *Xenopus* embryogenesis, Wnt/Fz signaling activates the small GTPase Rho (OMIM Ref. No. 165390), a key regulator of cytoskeleton architecture. Wnt/Fz activation of Rho requires the cytoplasmic protein dishevelled (DVL; OMIM Ref. No. 601365) and a novel formin (see OMIM Ref. No. 136535) homology (FH) protein that they identified and named DAAM1.

DAAM1 is a widely expressed protein that contains 1,078 amino acids and is identical to the KIAA0666 protein. Like other FH proteins, DAAM1 contains a central proline-rich

FH1 domain and a more C-terminal FH2 domain. The authors showed that DAAM1 binds to both DVL and Rho and mediates Wnt-induced DVL-Rho complex formation. Inhibition or depletion of DAAM1 prevented Wnt/Fz activation of Rho and of *Xenopus* gastrulation, but did not prevent activation of beta-catenin (OMIM Ref. No. 116806) signaling.

[16469] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16470] Habas, R.; Kato, Y.; He, X. : Wnt/Frizzled activation of Rho regulates vertebrate gastrulation and requires a novel Formin homology protein Daam1. *Cell* 107: 843–854, 2001. ; and

[16471] Ishikawa, K.; Nagase, T.; Suyama, M.; Miyajima, N.; Tanaka, A.; Kotani, H.; Nomura, N.; Ohara, O. : Prediction of the coding sequences of unidentified human genes. X. The complete sequ.

[16472] Further studies establishing the function and utilities of DAAM1 are found in John Hopkins OMIM database record ID 606626, and in cited publications numbered 452 and 9440 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Inositol

1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223) is another VGAM302 host target gene. ITPR2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR2 BINDING SITE, designated SEQ ID:7995, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16473] Another function of VGAM302 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 2 (ITPR2, Accession NM_002223). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR2. Neurocalcin Delta (NCALD, Accession NM_032041) is another VGAM302 host target gene. NCALD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NCALD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NCALD BINDING SITE, designated SEQ ID:25748, to the nucleotide sequence of

VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16474] Another function of VGAM302 is therefore inhibition of Neurocalcin Delta (NCALD, Accession NM_032041). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NCALD. Protein Phosphatase 2, Regulatory Subunit B (B56), Epsilon Isoform (PPP2R5E, Accession NM_006246) is another VGAM302 host target gene. PPP2R5E BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PPP2R5E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5E BINDING SITE, designated SEQ ID:12924, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16475] Another function of VGAM302 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Epsilon Isoform (PPP2R5E, Accession NM_006246), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM302 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with PPP2R5E. The function of PPP2R5E has been established by previous studies. is a regulatory subunit of protein phosphatase 2A involving in cellular processes such as cell cycle progression, growth factor signaling, and cell transformation.

[16476] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16477] McCright, B.; Brothman, A. R.; Virshup, D. M. : Assignment of human protein phosphatase 2A regulatory subunit genes B56-alpha, B56-beta, B56-gamma, B56-delta, and B56-epsilon (PPP2R5A--PPP2R5E), highly expressed in muscle and brain, to chromosome regions 1q41, 11q12, 3p21, 6p21.1, and 7p11.2-to-p12. Genomics 36: 168-170, 1996. ; and

[16478] McCright, B.; Rivers, A. M.; Audlin, S.; Virshup, D. M. : The B56 family of protein phosphatase 2A (PP2A) regulatory subunits encodes differentiation-induced phosphoproteins that target.

[16479] Further studies establishing the function and utilities of PPP2R5E are found in John Hopkins OMIM database record ID 601647, and in cited publications numbered 668 and

8305 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Ret Finger Protein (RFP, Accession NM_006510) is another VGAM302 host target gene. RFP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RFP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RFP BINDING SITE, designated SEQ ID:13263, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16480] Another function of VGAM302 is therefore inhibition of Ret Finger Protein (RFP, Accession NM_006510), a gene which involves in transcriptional regulation and may act in male germ cell development . Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RFP. The function of RFP has been established by previous studies. Ret finger protein (RFP) is a DNA-binding protein associated with the nuclear matrix (Isomura et al., 1992). Szpirer et al. (1997) demonstrated that, although the RFP gene and a gene for an olfactory receptor (OLF89) both map to

chromosome 6 less than 300 kb apart, the mouse homologs are located on 2 different chromosomes, namely 13 and 17, respectively. Thus the 2 genes delineate the breakpoint between 2 of the conserved synteny units on chromosome 6. Unit 1 (or UA) contains the major histocompatibility complex (MHC); unit 2 (or UB) contains the RFP gene. The mouse UA and UB regions are found on chromosome 17 and 13, respectively. The split at the UA/UB breakpoint must have occurred in the rodent lineage, before the mouse radiation, because the rat also shows nonsynteny of RFP and OLF89.

[16481] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16482] Isomura, T.; Tamiya-Koizumi, K.; Suzuki, M.; Yoshida, S.; Taniguchi, M.; Matsuyama, M.; Ishigaki, T.; Sakuma, S.; Takahashi, M. : RFP is a DNA binding protein associated with the nuclear matrix. *Nucleic Acids Res.* 20: 5305-5310, 1992. ; and

[16483] Szpirer, C.; Szpirer, J.; Riviere, M.; Tazi, R.; Pontarotti, P. : Mapping of the Olf89 and Rfp genes to the rat genome: comparison with the mouse and human and new insights into the evo.

[16484] Further studies establishing the function and utilities of RFP are found in John Hopkins OMIM database record ID 602165, and in cited publications numbered 6346–6347 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Slit Homolog 2 (Drosophila) (SLIT2, Accession NM_004787) is another VGAM302 host target gene. SLIT2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by SLIT2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLIT2 BINDING SITE, designated SEQ ID:11192, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16485] Another function of VGAM302 is therefore inhibition of Slit Homolog 2 (Drosophila) (SLIT2, Accession NM_004787). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLIT2. Son of Sevenless Homolog 2 (Drosophila) (SOS2, Accession XM_043720) is another VGAM302 host target gene. SOS2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated

region of mRNA encoded by SOS2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOS2 BINDING SITE, designated SEQ ID:34001, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16486] Another function of VGAM302 is therefore inhibition of Son of Sevenless Homolog 2 (Drosophila) (SOS2, Accession XM_043720). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOS2. Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM_015185) is another VGAM302 host target gene. ARHGEF9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF9 BINDING SITE, designated SEQ ID:17543, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16487] Another function of VGAM302 is therefore inhibition of Cdc42 Guanine Nucleotide Exchange Factor (GEF) 9 (ARHGEF9, Accession NM_015185). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF9. CIP29 (Accession NM_032364) is another VGAM302 host target gene. CIP29 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CIP29, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIP29 BINDING SITE, designated SEQ ID:26150, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16488] Another function of VGAM302 is therefore inhibition of CIP29 (Accession NM_032364). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIP29. DKFZP434N093 (Accession XM_086948) is another VGAM302 host target gene. DKFZP434N093 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434N093, correspond-

ing to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434N093 BINDING SITE, designated SEQ ID:38993, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16489] Another function of VGAM302 is therefore inhibition of DKFZP434N093 (Accession XM_086948). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434N093. Potassium Channel, Subfamily K, Member 13 (KCNK13, Accession NM_022054) is another VGAM302 host target gene. KCNK13 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNK13, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNK13 BINDING SITE, designated SEQ ID:22593, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16490] Another function of VGAM302 is therefore inhibition of Potassium Channel, Subfamily K, Member 13 (KCNK13,

Accession NM_022054). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNK13. KIAA0227 (Accession XM_027236) is another VGAM302 host target gene. KIAA0227 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0227, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0227 BINDING SITE, designated SEQ ID:30458, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16491] Another function of VGAM302 is therefore inhibition of KIAA0227 (Accession XM_027236). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0227. SENP7 (Accession NM_020654) is another VGAM302 host target gene. SENP7 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SENP7, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of SENP7 BINDING SITE, designated SEQ ID:21824, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16492] Another function of VGAM302 is therefore inhibition of SENP7 (Accession NM_020654). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SENP7. LOC151414 (Accession XM_087197) is another VGAM302 host target gene. LOC151414 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151414, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151414 BINDING SITE, designated SEQ ID:39111, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16493] Another function of VGAM302 is therefore inhibition of LOC151414 (Accession XM_087197). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151414. LOC253926 (Accession XM_170741) is an-

other VGAM302 host target gene. LOC253926 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253926 BINDING SITE, designated SEQ ID:45501, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16494] Another function of VGAM302 is therefore inhibition of LOC253926 (Accession XM_170741). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253926. LOC90826 (Accession XM_034321) is another VGAM302 host target gene. LOC90826 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90826, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90826 BINDING SITE, designated SEQ ID:32051, to the nucleotide sequence of VGAM302 RNA, herein designated VGAM RNA, also designated SEQ ID:3013.

[16495] Another function of VGAM302 is therefore inhibition of LOC90826 (Accession XM_034321). Accordingly, utilities of VGAM302 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90826. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 303 (VGAM303) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16496] VGAM303 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM303 was detected is described hereinabove with reference to Figs. 1–8.

[16497] VGAM303 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Epiphyas Postvittana Nucleopolyhedrovirus. VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16498] VGAM303 gene encodes a VGAM303 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM303

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM303 precursor RNA is designated SEQ ID:289, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:289 is located at position 103301 relative to the genome of Epi-phyas Postvittana Nucleopolyhedrovirus.

[16499] VGAM303 precursor RNA folds onto itself, forming VGAM303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16500] An enzyme complex designated DICER COMPLEX, `dices` the VGAM303 folded precursor RNA into VGAM303 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 42%) nucleotide sequence of VGAM303 RNA is designated SEQ ID:3014, and is provided hereinbelow with reference to the sequence listing part.

[16501] VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM303 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[16502] VGAM303 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM303 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM303 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16503] The complementary binding of VGAM303 RNA, herein designated VGAM RNA, to host target binding sites on VGAM303 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM303 host target RNA into VGAM303 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16504] It is appreciated that VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM303 host target genes. The mRNA of each one of this plurality of VGAM303 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM303 RNA, herein designated VGAM RNA, and which when bound by VGAM303 RNA causes inhibition of translation of respective one or more VGAM303 host target proteins.

[16505] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM303 gene, herein designated VGAM GENE, on one or more VGAM303 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16506] It is yet further appreciated that a function of VGAM303 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM303 include diagnosis, prevention and treatment of viral infection by Epiphyas Postvittana Nucleopolyhedrovirus. Specific functions, and accordingly utilities, of VGAM303 correlate with, and may be deduced from, the identity of the host target genes which VGAM303 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16507] Nucleotide sequences of the VGAM303 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM303 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM303 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM303 are further described hereinbelow with reference to Table 1.

[16508] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM303 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM303 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[16509] As mentioned hereinabove with reference to Fig. 1, a function of VGAM303 gene, herein designated VGAM is inhibition of expression of VGAM303 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM303 correlate with, and may be deduced from, the identity of the target genes which VGAM303 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16510] FLJ10579 (Accession NM_018145) is a VGAM303 host target gene. FLJ10579 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10579, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10579 BINDING SITE, designated SEQ ID:19942, to the nucleotide sequence of VGAM303 RNA, herein designated VGAM RNA, also designated SEQ ID:3014.

[16511] A function of VGAM303 is therefore inhibition of FLJ10579 (Accession NM_018145). Accordingly, utilities of VGAM303 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10579.

Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 304 (VGAM304) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16512] VGAM304 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM304 was detected is described hereinabove with reference to Figs. 1–8.

[16513] VGAM304 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16514] VGAM304 gene encodes a VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM304 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM304 precursor RNA is designated SEQ ID:290, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:290 is

located at position 86184 relative to the genome of Equine Herpesvirus 4.

[16515] VGAM304 precursor RNA folds onto itself, forming VGAM304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16516] An enzyme complex designated DICER COMPLEX, `dices` the VGAM304 folded precursor RNA into VGAM304 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM304 RNA is designated SEQ ID:3015, and is provided hereinbelow with reference to the sequence listing part.

[16517] VGAM304 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM304 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16518] VGAM304 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM304 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM304 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM304 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[16519] The complementary binding of VGAM304 RNA, herein designated VGAM RNA, to host target binding sites on VGAM304 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM304 host target RNA into VGAM304 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16520] It is appreciated that VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM304 host target genes. The mRNA of each one of this plurality of VGAM304 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM304 RNA, herein designated VGAM RNA, and which when bound by VGAM304 RNA causes inhibition of translation of respective one or more VGAM304

host target proteins.

[16521] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM304 gene, herein designated VGAM GENE, on one or more VGAM304 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16522] It is yet further appreciated that a function of VGAM304 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Spe-

cific functions, and accordingly utilities, of VGAM304 correlate with, and may be deduced from, the identity of the host target genes which VGAM304 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [16523] Nucleotide sequences of the VGAM304 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM304 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM304 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM304 are further described hereinbelow with reference to Table 1.
- [16524] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM304 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM304 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [16525] As mentioned hereinabove with reference to Fig. 1, a function of VGAM304 gene, herein designated VGAM is inhibition of expression of VGAM304 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM304 correlate with, and may be deduced from, the identity of the target genes which VGAM304 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16526] Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718) is a VGAM304 host target gene. BMP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BMP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BMP6 BINDING SITE, designated SEQ ID:7452, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16527] A function of VGAM304 is therefore inhibition of Bone Morphogenetic Protein 6 (BMP6, Accession NM_001718), a gene which induces cartilage and bone formation. Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BMP6. The function of BMP6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM233.Collagen, Type XV,

Alpha 1 (COL15A1, Accession NM_001855) is another VGAM304 host target gene. COL15A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by COL15A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL15A1 BINDING SITE, designated SEQ ID:7590, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16528] Another function of VGAM304 is therefore inhibition of Collagen, Type XV, Alpha 1 (COL15A1, Accession NM_001855), a gene which may be involved in maintaining the structure of connective tissue. Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL15A1. The function of COL15A1 has been established by previous studies. Undulin is a large glycoprotein of the interstitial extracellular matrix. It is restricted to dense and soft connective tissues and is associated with mature collagen fibrils (Schuppan et al., 1990). In SDS-polyacrylamide gels, undulin extracted from tissues has a molecular mass above 1,000 kD; under reducing condi-

tions, it migrates as 270-, 190-, and 180-kD polypeptides. By immunoscreening a human placenta cDNA expression library with antibodies against monkey undulin, Just et al. (1991) isolated 2 partial cDNAs, called UN1 and UN2, which encode the C-terminal portions of 2 undulin isoforms. The sequences of UN1 and UN2 are partly identical, and the authors suggested that they represent differentially spliced undulin transcripts. Northern blot analysis of human rhabdomyosarcoma cell poly(A) RNA using a probe specific for UN1 detected approximately 4.2-, 6.5-, and 8.5-kb transcripts; a probe specific for UN2 detected a single, approximately 5-kb transcript. The deduced polypeptides contain a differentially spliced von Willebrand factor (VWF; 193400) A domain and the type III homology domains found in fibronectin (OMIM Ref. No. 135600) and tenascin (OMIM Ref. No. 187380). Whereas UN1 has 7 complete and 1 truncated type III homology domains followed by a short proline-rich C-terminal segment, UN2 has 2 complete and 1 incomplete type III homologies followed by a unique acidic C-terminal domain. The authors stated that the mRNAs related to UN1 likely encode the major chains of the undulin molecule.

[16529] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [16530] Schuppan, D.; Cantaluppi, M. C.; Becker, J.; Veit, A.; Bunte, T.; Troyer, D.; Schuppan, F.; Schmid, M.; Ackermann, R.; Hahn, E. G. : Undulin, an extracellular matrix glycoprotein associated with collagen fibrils. J. Biol. Chem. 265: 8823–8832, 1990. ; and
- [16531] Just, M.; Herbst, H.; Hummel, M.; Durkop, H.; Tripier, D.; Stein, H.; Schuppan, D. : Undulin is a novel member of the fibronectin–tenascin family of extracellular matrix glycoproteins. J.
- [16532] Further studies establishing the function and utilities of COL15A1 are found in John Hopkins OMIM database record ID 120325, and in cited publications numbered 12014–12025 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Paired Box Gene 7 (PAX7, Accession NM_013945) is another VGAM304 host target gene. PAX7 BINDING SITE1 and PAX7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PAX7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se–

quences of PAX7 BINDING SITE1 and PAX7 BINDING SITE2, designated SEQ ID:15133 and SEQ ID:8445 respectively, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16533] Another function of VGAM304 is therefore inhibition of Paired Box Gene 7 (PAX7, Accession NM_013945), a gene which involves in myogenesis. Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PAX7. The function of PAX7 has been established by previous studies. In a review of 28 published cases of the pediatric soft tissue cancer alveolar rhabdomyosarcoma (OMIM Ref. No. 268220), Whang-Peng et al. (1992) found a characteristic t(2;13)(q35;q14) translocation and a variant t(1;13)(p36;q14) translocation in 64% and 18% of the cases, respectively. Subsequent molecular biology studies demonstrated that these translocations fuse the PAX3 gene (OMIM Ref. No. 193500) on chromosome 2 or the PAX7 gene on chromosome 1 with the forkhead in rhabdomyosarcoma gene (OMIM Ref. No. 136533) on chromosome 13 to generate PAX3/FKHR or PAX7/FKHR fusion genes. These genes encode chimeric transcription factors which, in the case of PAX3/FKHR, was shown to activate

excessively transcription from binding targets of the wild-type PAX3 transcription factor. Using FISH, RT-PCR, and quantitative Southern blot analyses, Barr et al. (1996) demonstrated that these fusion genes are amplified in 20% of fusion-positive tumors. In particular, they found in vivo amplification of these fusions in 1 of 22 PAX3/FKHR-positive cases and 5 of 7 PAX7/FKHR-positive cases. By representational difference analysis, Seale et al. (2000) isolated mouse Pax7 as a gene specifically expressed in cultured satellite cell-derived myoblasts. In situ hybridization revealed that Pax7 is also expressed in satellite cells residing in adult muscle. Cell culture and electron microscopic analysis showed a complete absence of satellite cells in Pax7 $-/-$ skeletal muscle. Surprisingly, fluorescence-activated cell sorting analysis indicated that the proportion of muscle-derived stem cells was unaffected. Stem cells from Pax7 $-/-$ muscle displayed an almost 10-fold increase in their ability to form hematopoietic colonies. These results demonstrated that satellite cells and muscle-derived stem cells represent distinct cell populations. Furthermore, these studies suggested that induction of Pax7 in muscle-derived stem cells induces satellite cell specification by restricting alternate develop-

mental programs. Animal model experiments lend further support to the function of PAX7. By representational difference analysis, Seale et al. (2000) isolated mouse Pax7 as a gene specifically expressed in cultured satellite cell-derived myoblasts. In situ hybridization revealed that Pax7 is also expressed in satellite cells residing in adult muscle. Cell culture and electron microscopic analysis showed a complete absence of satellite cells in Pax7 $-/-$ skeletal muscle. Surprisingly, fluorescence-activated cell sorting analysis indicated that the proportion of muscle-derived stem cells was unaffected. Stem cells from Pax7 $-/-$ muscle displayed an almost 10-fold increase in their ability to form hematopoietic colonies. These results demonstrated that satellite cells and muscle-derived stem cells represent distinct cell populations. Furthermore, these studies suggested that induction of Pax7 in muscle-derived stem cells induces satellite cell specification by restricting alternate developmental programs.

[16534] It is appreciated that the abovementioned animal model for PAX7 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16535] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [16536] Barr, F. G.; Nauta, L. E.; Davis, R. J.; Schafer, B. W.; Nycum, L. M.; Biegel, J. A. : In vivo amplification of the PAX3–FKHR and PAX7–FKHR fusion genes in alveolar rhabdomyosarcoma. *Hum. Molec. Genet.* 5: 15–21, 1996. ; and
- [16537] Seale, P.; Sabourin, L. A.; Girgis–Gabardo, A.; Mansouri, A.; Gruss, P.; Rudnicki, M. A. : Pax7 is required for the specification of myogenic satellite cells. *Cell* 102: 777–786, 2000.
- [16538] Further studies establishing the function and utilities of PAX7 are found in John Hopkins OMIM database record ID 167410, and in cited publications numbered 10719–10721, 10338, 10722–1072 and 10714 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. BCL2–like 1 (BCL2L1, Accession NM_138578) is another VGAM304 host target gene. BCL2L1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by BCL2L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL2L1 BINDING SITE, designated SEQ

ID:28895, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16539] Another function of VGAM304 is therefore inhibition of BCL2-like 1 (BCL2L1, Accession NM_138578). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL2L1. Chromosome 20 Open Reading Frame 98 (C20orf98, Accession XM_049398) is another VGAM304 host target gene. C20orf98 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C20orf98, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf98 BINDING SITE, designated SEQ ID:35413, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16540] Another function of VGAM304 is therefore inhibition of Chromosome 20 Open Reading Frame 98 (C20orf98, Accession XM_049398). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf98. DK-

FZp547O146 (Accession NM_020224) is another VGAM304 host target gene. DKFZp547O146 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp547O146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp547O146 BINDING SITE, designated SEQ ID:21484, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16541] Another function of VGAM304 is therefore inhibition of DKFZp547O146 (Accession NM_020224). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp547O146. FLJ11539 (Accession NM_024748) is another VGAM304 host target gene. FLJ11539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ11539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11539 BINDING SITE, designated SEQ ID:24085, to the nucleotide sequence of VGAM304 RNA, herein designated

VGAM RNA, also designated SEQ ID:3015.

[16542] Another function of VGAM304 is therefore inhibition of FLJ11539 (Accession NM_024748). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11539. Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_017744) is another VGAM304 host target gene. ST7L BINDING SITE1 through ST7L BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ST7L, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ST7L BINDING SITE1 through ST7L BINDING SITE3, designated SEQ ID:19334, SEQ ID:28976 and SEQ ID:29206 respectively, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16543] Another function of VGAM304 is therefore inhibition of Suppression of Tumorigenicity 7 Like (ST7L, Accession NM_017744). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ST7L. Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023) is an–

other VGAM304 host target gene. ZFP91 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZFP91, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZFP91 BINDING SITE, designated SEQ ID:27578, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also designated SEQ ID:3015.

[16544] Another function of VGAM304 is therefore inhibition of Zinc Finger Protein 91 Homolog (mouse) (ZFP91, Accession NM_053023). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZFP91. LOC150157 (Accession XM_097823) is another VGAM304 host target gene. LOC150157 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150157, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150157 BINDING SITE, designated SEQ ID:41142, to the nucleotide sequence of VGAM304 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3015.

[16545] Another function of VGAM304 is therefore inhibition of LOC150157 (Accession XM_097823). Accordingly, utilities of VGAM304 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150157. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 305 (VGAM305) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16546] VGAM305 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM305 was detected is described hereinabove with reference to Figs. 1–8.

[16547] VGAM305 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16548] VGAM305 gene encodes a VGAM305 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM305 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM305 precursor RNA is designated SEQ ID:291, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:291 is located at position 85065 relative to the genome of Equine Herpesvirus 4.

[16549] VGAM305 precursor RNA folds onto itself, forming VGAM305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16550] An enzyme complex designated DICER COMPLEX, `dices` the VGAM305 folded precursor RNA into VGAM305 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 42%) nucleotide sequence of VGAM305 RNA is designated SEQ ID:3016, and is provided hereinbelow with reference to the sequence listing part.

[16551] VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM305 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16552] VGAM305 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM305 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM305 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16553] The complementary binding of VGAM305 RNA, herein designated VGAM RNA, to host target binding sites on VGAM305 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM305 host target RNA into VGAM305 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16554] It is appreciated that VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM305 host target genes. The mRNA of

each one of this plurality of VGAM305 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM305 RNA, herein designated VGAM RNA, and which when bound by VGAM305 RNA causes inhibition of translation of respective one or more VGAM305 host target proteins.

[16555] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM305 gene, herein designated VGAM GENE, on one or more VGAM305 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[16556] It is yet further appreciated that a function of VGAM305 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM305 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM305 correlate with, and may be deduced from, the identity of the host target genes which VGAM305 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16557] Nucleotide sequences of the VGAM305 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM305 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM305 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM305 are further described hereinbelow with reference to Table 1.

[16558] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM305 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM305 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[16559] As mentioned hereinabove with reference to Fig. 1, a function of VGAM305 gene, herein designated VGAM is inhibition of expression of VGAM305 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM305 correlate with, and may be deduced from, the identity of the target genes which VGAM305 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16560] CD5 Antigen (p56-62) (CD5, Accession NM_014207) is a VGAM305 host target gene. CD5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD5 BINDING SITE, designated SEQ ID:15476, to the nucleotide sequence of VGAM305 RNA, herein designated VGAM RNA, also designated SEQ ID:3016.

[16561] A function of VGAM305 is therefore inhibition of CD5 Antigen (p56-62) (CD5, Accession NM_014207). Accordingly, utilities of VGAM305 include diagnosis, prevention

and treatment of diseases and clinical conditions associated with CD5. LOC148930 (Accession XM_086369) is another VGAM305 host target gene. LOC148930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148930 BINDING SITE, designated SEQ ID:38618, to the nucleotide sequence of VGAM305 RNA, herein designated VGAM RNA, also designated SEQ ID:3016.

[16562] Another function of VGAM305 is therefore inhibition of LOC148930 (Accession XM_086369). Accordingly, utilities of VGAM305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148930. LOC158310 (Accession XM_098919) is another VGAM305 host target gene. LOC158310 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC158310, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158310 BINDING SITE, designated SEQ ID:41944, to

the nucleotide sequence of VGAM305 RNA, herein designated VGAM RNA, also designated SEQ ID:3016.

[16563] Another function of VGAM305 is therefore inhibition of LOC158310 (Accession XM_098919). Accordingly, utilities of VGAM305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158310. LOC256950 (Accession XM_170922) is another VGAM305 host target gene. LOC256950 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256950, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256950 BINDING SITE, designated SEQ ID:45699, to the nucleotide sequence of VGAM305 RNA, herein designated VGAM RNA, also designated SEQ ID:3016.

[16564] Another function of VGAM305 is therefore inhibition of LOC256950 (Accession XM_170922). Accordingly, utilities of VGAM305 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256950. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Ad-

dress Messenger 306 (VGAM306) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16565] VGAM306 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM306 was detected is described hereinabove with reference to Figs. 1–8.

[16566] VGAM306 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Equine Herpesvirus 4. VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16567] VGAM306 gene encodes a VGAM306 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM306 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM306 precursor RNA is designated SEQ ID:292, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:292 is located at position 87168 relative to the genome of Equine Herpesvirus 4.

[16568] VGAM306 precursor RNA folds onto itself, forming VGAM306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16569] An enzyme complex designated DICER COMPLEX, `dices` the VGAM306 folded precursor RNA into VGAM306 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 45%) nucleotide sequence of VGAM306 RNA is designated SEQ ID:3017, and is provided hereinbelow with reference to the sequence listing part.

[16570] VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM306 host target RNA, herein designated VGAM

HOST TARGET RNA. VGAM306 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16571] VGAM306 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM306 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM306 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding

sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16572] The complementary binding of VGAM306 RNA, herein designated VGAM RNA, to host target binding sites on VGAM306 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM306 host target RNA into VGAM306 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16573] It is appreciated that VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM306 host target genes. The mRNA of each one of this plurality of VGAM306 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM306 RNA, herein designated VGAM RNA, and which when bound by VGAM306 RNA causes inhibition of translation of respective one or more VGAM306 host target proteins.

[16574] It is further appreciated by one skilled in the art that the

mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM306 gene, herein designated VGAM GENE, on one or more VGAM306 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16575] It is yet further appreciated that a function of VGAM306 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of viral infection by Equine Herpesvirus 4. Specific functions, and accordingly utilities, of VGAM306 correlate with, and may be deduced from, the identity of the

host target genes which VGAM306 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [16576] Nucleotide sequences of the VGAM306 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM306 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM306 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM306 are further described hereinbelow with reference to Table 1.
- [16577] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM306 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM306 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [16578] As mentioned hereinabove with reference to Fig. 1, a function of VGAM306 gene, herein designated VGAM is inhibition of expression of VGAM306 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM306 correlate with, and may be deduced from, the identity of the target genes which VGAM306

binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16579] CD28 Antigen (Tp44) (CD28, Accession NM_006139) is a VGAM306 host target gene. CD28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CD28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CD28 BINDING SITE, designated SEQ ID:12785, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16580] A function of VGAM306 is therefore inhibition of CD28 Antigen (Tp44) (CD28, Accession NM_006139), a gene which possibly involved in t-cell activation. Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CD28. The function of CD28 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM281. Membrane Protein, Palmitoylated 5 (MAGUK p55 subfamily member 5) (MPP5, Accession NM_022474) is another VGAM306 host target gene. MPP5

BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MPP5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MPP5 BINDING SITE, designated SEQ ID:22840, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16581] Another function of VGAM306 is therefore inhibition of Membrane Protein, Palmitoylated 5 (MAGUK p55 subfamily member 5) (MPP5, Accession NM_022474), a gene which may regulate transmembrane proteins that bind calcium, calmodulin, or nucleotides. Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MPP5. The function of MPP5 has been established by previous studies. Members of the peripheral membrane-associated guanylate kinase (MAGUK) family function in tumor suppression and receptor clustering by forming multiprotein complexes containing distinct sets of transmembrane, cytoskeletal, and cytoplasmic signaling proteins. All MAGUKs contain a PDZ-SH3-GUK core and are divided into 4 subfamilies, DLG-like (see OMIM Ref. No. DLG1;

601014), ZO1-like (see OMIM Ref. No. TJP1; 601009), p55-like (see OMIM Ref. No. MPP1; 305360), and LIN2-like (see OMIM Ref. No. CASK; 300172), based on their size and the presence of additional domains (Tseng et al., 2001). MPP5 is a member of the p55-like MAGUK subfamily. Kamberov et al. (2000) cloned and characterized the mouse Mpp5 and Mpp6 (OMIM Ref. No. 606959) genes, which they called Pals1 and Pals2, respectively. The Pals proteins bind to mouse Lin7 (OMIM Ref. No. 603380) through a region N-terminal to their PDZ domains. Roh et al. (2002) showed that Pals1 contains 2 Lin2 (OMIM Ref. No. 300172)/Lin7-binding domains, which they called L27 domains, N-terminal to the PDZ domain. The C-terminal L27 domain, L27C, binds Lin7, whereas the N-terminal L27 domain, L27N, targets Pals1 to tight junctions by binding to Patj (INAD; 603199) and to Crb1 (OMIM Ref. No. 604210).

[16582] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16583] Roh, M. H.; Makarova, O.; Liu, C.-J.; Shin, K.; Lee, S.; Laurenc, S.; Goyal, M.; Wiggins, R.; Margolis, B. : The Maguk protein, Pals1, functions as an adapter, linking mam-

malian homologues of Crumbs and Discs Lost. J. Cell Biol. 157: 161–172, 2002. ; and

[16584] Tseng, T.–C.; Marfatia, S. M.; Bryant, P. J.; Pack, S.; Zhuang, A.; O'Brien, J. E.; Lin, L.; Hanada, T.; Chishti, A. H. : VAM–1: a new member of the MAGUK family binds to human Veli–1.

[16585] Further studies establishing the function and utilities of MPP5 are found in John Hopkins OMIM database record ID 606958, and in cited publications numbered 513 and 7979–5140 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phosphoinositide–3–kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM_002646) is another VGAM306 host target gene. PIK3C2B BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PIK3C2B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3C2B BINDING SITE, designated SEQ ID:8510, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16586] Another function of VGAM306 is therefore inhibition of

Phosphoinositide-3-kinase, Class 2, Beta Polypeptide (PIK3C2B, Accession NM_002646). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3C2B. DKFZP727C091 (Accession XM_038689) is another VGAM306 host target gene. DKFZP727C091 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZP727C091, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP727C091 BINDING SITE, designated SEQ ID:32908, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16587] Another function of VGAM306 is therefore inhibition of DKFZP727C091 (Accession XM_038689). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP727C091. Dickkopf Homolog 3 (*Xenopus laevis*) (DKK3, Accession NM_013253) is another VGAM306 host target gene. DKK3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKK3, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKK3 BINDING SITE, designated SEQ ID:14924, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16588] Another function of VGAM306 is therefore inhibition of Dickkopf Homolog 3 (*Xenopus laevis*) (DKK3, Accession NM_013253). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKK3. KIAA0323 (Accession XM_032634) is another VGAM306 host target gene. KIAA0323 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0323, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0323 BINDING SITE, designated SEQ ID:31698, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16589] Another function of VGAM306 is therefore inhibition of KIAA0323 (Accession XM_032634). Accordingly, utilities

of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0323. KIAA1023 (Accession NM_017604) is another VGAM306 host target gene. KIAA1023 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1023, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1023 BINDING SITE, designated SEQ ID:19099, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16590] Another function of VGAM306 is therefore inhibition of KIAA1023 (Accession NM_017604). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1023. KIAA1196 (Accession XM_028968) is another VGAM306 host target gene. KIAA1196 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1196, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

KIAA1196 BINDING SITE, designated SEQ ID:30824, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16591] Another function of VGAM306 is therefore inhibition of KIAA1196 (Accession XM_028968). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1196. LOC112817 (Accession NM_138413) is another VGAM306 host target gene. LOC112817 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112817, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112817 BINDING SITE, designated SEQ ID:28784, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16592] Another function of VGAM306 is therefore inhibition of LOC112817 (Accession NM_138413). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112817. LOC253675 (Accession XM_172990) is another VGAM306 host target gene. LOC253675 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253675, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253675 BINDING SITE, designated SEQ ID:46269, to the nucleotide sequence of VGAM306 RNA, herein designated VGAM RNA, also designated SEQ ID:3017.

[16593] Another function of VGAM306 is therefore inhibition of LOC253675 (Accession XM_172990). Accordingly, utilities of VGAM306 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253675. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 307 (VGAM307) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16594] VGAM307 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM307 was detected is described hereinabove with reference to Figs. 1-8.

[16595] VGAM307 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Adenovirus E. VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16596] VGAM307 gene encodes a VGAM307 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM307 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM307 precursor RNA is designated SEQ ID:293, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:293 is located at position 1062 relative to the genome of Human Adenovirus E.

[16597] VGAM307 precursor RNA folds onto itself, forming VGAM307 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[16598] An enzyme complex designated DICER COMPLEX, `dices` the VGAM307 folded precursor RNA into VGAM307 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 77%) nucleotide sequence of VGAM307 RNA is designated SEQ ID:3018, and is provided hereinbelow with reference to the sequence listing part.

[16599] VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM307 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16600] VGAM307 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM307 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM307 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM307 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[16601] The complementary binding of VGAM307 RNA, herein designated VGAM RNA, to host target binding sites on VGAM307 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM307 host target RNA into VGAM307 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16602] It is appreciated that VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM307 host target genes. The mRNA of each one of this plurality of VGAM307 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM307 RNA, herein designated VGAM RNA, and which when bound by VGAM307 RNA causes inhibition of translation of respective one or more VGAM307 host target proteins.

[16603] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM307 gene, herein designated VGAM GENE, on one or more VGAM307 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16604] It is yet further appreciated that a function of VGAM307 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of viral infection by Human Adenovirus E. Specific functions, and accordingly utilities, of VGAM307 correlate with, and may be deduced from, the identity of the host target genes which VGAM307 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16605] Nucleotide sequences of the VGAM307 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM307 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM307 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM307 are further described hereinbelow with reference to Table 1.

[16606] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM307 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM307 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16607] As mentioned hereinabove with reference to Fig. 1, a function of VGAM307 gene, herein designated VGAM is inhibition of expression of VGAM307 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM307 correlate with, and may be deduced from, the identity of the target genes which VGAM307 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16608] Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147) is a VGAM307 host target gene. EIF1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of EIF1A BINDING SITE, designated SEQ ID:42717, to the nucleotide sequence of VGAM307 RNA, herein designated VGAM RNA, also designated SEQ ID:3018.

[16609] A function of VGAM307 is therefore inhibition of Eukaryotic Translation Initiation Factor 1A (EIF1A, Accession XM_114147), a gene which seems to be required for maximal rate of protein biosynthesis. Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EIF1A. The function of EIF1A and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM120. DNA Cross-link Repair 1A (PSO2 homolog, *S. cerevisiae*) (DCLRE1A, Accession XM_044815) is another VGAM307 host target gene. DCLRE1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DCLRE1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DCLRE1A BINDING SITE, designated SEQ ID:34279, to the nucleotide sequence of VGAM307 RNA, herein designated VGAM

RNA, also designated SEQ ID:3018.

[16610] Another function of VGAM307 is therefore inhibition of DNA Cross-link Repair 1A (PSO2 homolog, *S. cerevisiae*) (DCLRE1A, Accession XM_044815). Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DCLRE1A. FLJ31737 (Accession NM_144984) is another VGAM307 host target gene. FLJ31737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ31737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31737 BINDING SITE, designated SEQ ID:29588, to the nucleotide sequence of VGAM307 RNA, herein designated VGAM RNA, also designated SEQ ID:3018.

[16611] Another function of VGAM307 is therefore inhibition of FLJ31737 (Accession NM_144984). Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31737. LOC145134 (Accession XM_096722) is another VGAM307 host target gene. LOC145134 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of

mRNA encoded by LOC145134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145134 BINDING SITE, designated SEQ ID:40499, to the nucleotide sequence of VGAM307 RNA, herein designated VGAM RNA, also designated SEQ ID:3018.

[16612] Another function of VGAM307 is therefore inhibition of LOC145134 (Accession XM_096722). Accordingly, utilities of VGAM307 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145134. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 308 (VGAM308) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16613] VGAM308 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM308 was detected is described hereinabove with reference to Figs. 1–8.

[16614] VGAM308 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Paramecium Bursaria Chlorella Virus 1. VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16615] VGAM308 gene encodes a VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM308 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM308 precursor RNA is designated SEQ ID:294, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:294 is located at position 260067 relative to the genome of Paramecium Bursaria Chlorella Virus 1.

[16616] VGAM308 precursor RNA folds onto itself, forming VGAM308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16617] An enzyme complex designated DICER COMPLEX, `dices` the VGAM308 folded precursor RNA into VGAM308 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 79%) nucleotide sequence of VGAM308 RNA is designated SEQ ID:3019, and is provided hereinbelow with reference to the sequence listing part.

[16618] VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM308 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16619] VGAM308 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM308 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM308 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16620] The complementary binding of VGAM308 RNA, herein designated VGAM RNA, to host target binding sites on VGAM308 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM308 host tar-

get RNA into VGAM308 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16621] It is appreciated that VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM308 host target genes. The mRNA of each one of this plurality of VGAM308 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM308 RNA, herein designated VGAM RNA, and which when bound by VGAM308 RNA causes inhibition of translation of respective one or more VGAM308 host target proteins.

[16622] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM308 gene, herein designated VGAM GENE, on one or more VGAM308 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16623] It is yet further appreciated that a function of VGAM308 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM308 include diagnosis, prevention and treatment of viral infection by Paramecium Bursaria Chlorella Virus 1. Specific functions, and accordingly utilities, of VGAM308 correlate with, and may be deduced from, the identity of the host target genes which VGAM308 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16624] Nucleotide sequences of the VGAM308 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM308 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM308 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM308 are further

described hereinbelow with reference to Table 1.

[16625] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM308 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM308 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16626] As mentioned hereinabove with reference to Fig. 1, a function of VGAM308 gene, herein designated VGAM is inhibition of expression of VGAM308 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM308 correlate with, and may be deduced from, the identity of the target genes which VGAM308 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16627] Transcription Factor 12 (HTF4, helix-loop-helix transcription factors 4) (TCF12, Accession NM_003205) is a VGAM308 host target gene. TCF12 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCF12, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of TCF12 BINDING SITE, designated SEQ ID:9202, to the nucleotide sequence of VGAM308 RNA, herein designated VGAM RNA, also designated SEQ ID:3019.

[16628] A function of VGAM308 is therefore inhibition of Transcription Factor 12 (HTF4, helix-loop-helix transcription factors 4) (TCF12, Accession NM_003205), a gene which may play important roles during development of the nervous system as well as in other organ systems. Accordingly, utilities of VGAM308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCF12. The function of TCF12 has been established by previous studies. A partial cDNA for HTF4 was obtained by Zhang et al. (1991) which predicted a protein that is a member of the class A basic helix-loop-helix (bHLH) family. The same cDNA, designated HEB, was cloned by Hu et al. (1992). Based on studies of the mouse and chicken cDNAs, Zhang and Bina (1992) proposed that transcripts of HTF4 can be differentially spliced to yield distinct but related proteins which are evolutionarily similar to the products of the E2A gene, also known as transcription factor 3 (TCF3; 147141). In vitro assays have shown that HTF4 can form heterodimers with other bHLH

proteins of class A (e.g., OMIM Ref. No. 147141) and class B (e.g., the myogenic factors; MYF3, 159970; MYF5, 159990; and MYF6, 159991), as well as the inhibitor of DNA binding (ID1; 600349) and stem cell leukemia hematopoietic transcription factor (TAL1; 187040). In DNA binding assays, complexes of HTF4 with the myogenic factors have a relatively high affinity for the E box motifs of the mE2 (OMIM Ref. No. CACGTG) and kappa E2/muE5 (OMIM Ref. No. CACCTG) types, whereas heterodimers of HTF4 and TAL1 interact poorly (Doyle et al., 1994). These results and those obtained from transient expression studies indicated to the authors that leukemogenesis caused by TAL1 might include a pathway where TAL1 would act as a negative regulator of gene expression by forming a complex with class A bHLH proteins. Zhang et al. (1995) used a panel of somatic cell hybrids to map HTF4 to chromosome 15. By fluorescence in situ hybridization, they further localized the gene to 15q21. By Northern blot analysis, Zhang et al. (1995) showed that TCF12 is expressed, at varying levels, in many human cell lines and tissues. High levels of transcription in Jurkat cells support the view that TCF12 gene products may play a central role in T cell regulation (Hu et al., 1992; Sawada

and Littman, 1993; and Doyle et al., 1994), and detection of the mRNA in human heart and skeletal muscle supports a role for TCF12 in myogenesis.

[16629] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16630] Doyle, K.; Zhang, Y.; Baer, R.; Bina, M. : Distinguishable patterns of protein–DNA interactions involving complexes of basic helix–loop–helix proteins. J. Biol. Chem. 269: 12099–12105, 1994. ; and

[16631] Zhang, Y.; Flejter, W. L.; Barcroft, C. L.; Riviere, M.; Szpirer, J.; Szpirer, C.; Bina, M. : Localization of the human HTF4 transcription factors 4 gene (TCF12) to chromosome 15q21. C.

[16632] Further studies establishing the function and utilities of TCF12 are found in John Hopkins OMIM database record ID 600480, and in cited publications numbered 9519–9524 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476) is another VGAM308 host target gene. BTN2A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

BTN2A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN2A1 BINDING SITE, designated SEQ ID:27802, to the nucleotide sequence of VGAM308 RNA, herein designated VGAM RNA, also designated SEQ ID:3019.

[16633] Another function of VGAM308 is therefore inhibition of Butyrophilin, Subfamily 2, Member A1 (BTN2A1, Accession NM_078476). Accordingly, utilities of VGAM308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN2A1. PP35 (Accession NM_007016) is another VGAM308 host target gene. PP35 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PP35, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PP35 BINDING SITE, designated SEQ ID:13872, to the nucleotide sequence of VGAM308 RNA, herein designated VGAM RNA, also designated SEQ ID:3019.

[16634] Another function of VGAM308 is therefore inhibition of PP35 (Accession NM_007016). Accordingly, utilities of

VGAM308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PP35.

LOC159121 (Accession XM_099028) is another VGAM308 host target gene. LOC159121 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC159121, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC159121 BINDING SITE, designated SEQ ID:42062, to the nucleotide sequence of VGAM308 RNA, herein designated VGAM RNA, also designated SEQ ID:3019.

[16635] Another function of VGAM308 is therefore inhibition of LOC159121 (Accession XM_099028). Accordingly, utilities of VGAM308 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC159121. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 309 (VGAM309) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16636] VGAM309 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM309 was detected is described hereinabove with reference to Figs. 1–8.

[16637] VGAM309 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 6. VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16638] VGAM309 gene encodes a VGAM309 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM309 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM309 precursor RNA is designated SEQ ID:295, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:295 is located at position 15267 relative to the genome of Human Herpesvirus 6.

[16639] VGAM309 precursor RNA folds onto itself, forming VGAM309 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16640] An enzyme complex designated DICER COMPLEX, `dices` the VGAM309 folded precursor RNA into VGAM309 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 72%) nucleotide sequence of VGAM309 RNA is designated SEQ ID:3020, and is provided hereinbelow with reference to the sequence listing part.

[16641] VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM309 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[16642] VGAM309 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM309 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM309 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16643] The complementary binding of VGAM309 RNA, herein designated VGAM RNA, to host target binding sites on VGAM309 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM309 host target RNA into VGAM309 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16644] It is appreciated that VGAM309 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM309 host target genes. The mRNA of each one of this plurality of VGAM309 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM309 RNA, herein designated VGAM RNA, and which when bound by VGAM309 RNA causes inhibition of translation of respective one or more VGAM309 host target proteins.

[16645] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM309 gene, herein designated VGAM GENE, on one or more VGAM309 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16646] It is yet further appreciated that a function of VGAM309 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 6. Specific functions, and accordingly utilities, of VGAM309 correlate with, and may be deduced from, the identity of the host target genes which VGAM309 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16647] Nucleotide sequences of the VGAM309 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM309 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM309 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM309 are further
described hereinbelow with reference to Table 1.

[16648] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM309 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM309 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[16649] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM309 gene, herein designated VGAM is
inhibition of expression of VGAM309 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM309 correlate with, and may be deduced
from, the identity of the target genes which VGAM309
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[16650] Frizzled Homolog 4 (Drosophila) (FZD4, Accession
NM_012193) is a VGAM309 host target gene. FZD4 BIND-

ING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FZD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FZD4 BINDING SITE, designated SEQ ID:14487, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16651] A function of VGAM309 is therefore inhibition of Frizzled Homolog 4 (Drosophila) (FZD4, Accession NM_012193), a gene which may function in cell polarity, cell fate specification and cancer; similar to frizzled receptor family, has seven transmembrane domains. Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FZD4. The function of FZD4 has been established by previous studies. Members of the 'frizzled' (FZ) gene family (see OMIM Ref. No. 601766) encode 7-transmembrane domain proteins that are receptors for Wnt (see OMIM Ref. No. 164975) signaling proteins. By screening a human fetal lung cDNA library with an FZD4 cDNA fragment isolated from a human gastric cancer cDNA pool, Kirikoshi et al. (1999) obtained a full-length cDNA of FZD4. FZD4 en-

codes a deduced 537-amino acid protein that has a cysteine-rich domain in the N-terminal extracellular region, 2 cysteine residues in the second and third extracellular loops, 2 N-linked glycosylation extracellular sites, and the S/T-X-V motif in the C terminus. Amino acid sequence identity with other FZD proteins ranged from 39 to 52% in the N terminus to 42 to 69% in the transmembrane domains. Northern blot analysis revealed expression of a 7.7-kb transcript in large amounts in adult heart, skeletal muscle, ovary, and fetal kidney, in moderate amounts in adult liver, kidney, pancreas, spleen, and fetal lung, and in small amounts in placenta, adult lung, prostate, testis, colon, fetal brain, and liver. Expression was also strong in HeLa cells but not in several cancer cell lines. Familial exudative vitreoretinopathy (FEVR) is a hereditary ocular disorder characterized by a failure of peripheral retinal vascularization. Loci associated with FEVR map to 11q13-q23 (EVR1; 133780), Xp11.4 (EVR2; 305390), and 11p13-p12 (EVR3; 605750). In a large Canadian family of British descent, Robitaille et al. (2002) demonstrated linkage to 11q13-q23 for autosomal dominant FEVR and refined the disease locus to a genomic region spanning 1.55 Mb. The region contained the FZD4 gene, which they subjected to

mutation search and identified in affected individuals a deletion of 6 nucleotides, 1479–1484, resulting in deletion of 2 highly conserved amino acids, met493 and trp494. In a second small family they found a deletion of 2 nucleotides, 1501–1502, that resulted in a frameshift at leu501, creating a stop codon at residue 533. Both mutations were located in exon 2 and altered the seventh transmembrane domain and the intracellular carboxy-terminal tail, respectively. No mutations in FZD4 were detected in 3 other small families with FEVR. Robitaille et al. (2002) presented data indicating that the changes in FZD4 in these families with autosomal dominant FEVR represented loss of function mutations.

[16652] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16653] Kirikoshi, H.; Sagara, N.; Koike, J.; Tanaka, K.; Sekihara, H.; Hirai, M.; Katoh, M. : Molecular cloning and characterization of human frizzled-4 on chromosome 11q14-q21. Biochem. Biophys. Res. Commun. 264: 955–961, 1999. ; and

[16654] Robitaille, J.; MacDonald, M. L. E.; Kaykas, A.; Sheldahl, L. C.; Zeisler, J.; Dube, M.-P.; Zhang, L.-H.; Singaraja, R. R.;

Guernsey, D. L.; Zhang, B.; Siebert, L. F.; Hoskin-Mott, A.;

[16655] Further studies establishing the function and utilities of FZD4 are found in John Hopkins OMIM database record ID 604579, and in cited publications numbered 493 and 4941 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neuropeptide Y Receptor Y2 (NPY2R, Accession NM_000910) is another VGAM309 host target gene. NPY2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NPY2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NPY2R BINDING SITE, designated SEQ ID:6610, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16656] Another function of VGAM309 is therefore inhibition of Neuropeptide Y Receptor Y2 (NPY2R, Accession NM_000910), a gene which stimulates intracellular calcium flux and may modulate psychomotor activity, food intake, endocrine secretion and vasoconstriction. Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associ-

ated with NPY2R. The function of NPY2R has been established by previous studies. Neuropeptide Y (NPY) signals through a family of G protein-coupled receptors present in the brain and sympathetic neurons. At least 3 types of neuropeptide Y receptor have been defined on the basis of pharmacologic criteria, tissue distribution, and structure of the encoding gene; see 162641 and 162643. Rose et al. (1995) reported the expression cloning in COS cells of a cDNA for the human type 2 receptor, NPY2R. Transfected cells showed high affinity for NPY (OMIM Ref. No. 162640), peptide YY (PYY; 600781), and a fragment of NPY including amino acids 13 to 36. The predicted 381-amino acid protein has 7 transmembrane domains characteristic of G protein-coupled receptors and is only 31% identical to the human Y1 receptor (NPY1R; 162641). A 4-kb mRNA was detected on Northern blots of tissue samples from several regions of the nervous system. Gerald et al. (1995) cloned the cDNA corresponding to the human Y2 receptor from a human hippocampal cDNA expression library using a radiolabeled PYY-binding assay. They expressed the Y2 gene in COS-7 cells and performed a hormone-binding assay which showed that the Y2 receptor binds (from highest to lowest affinity) PYY, NPY,

and pancreatic polypeptide (PP; 167780) hormones.

[16657] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16658] Gerald, C.; Walker, M. W.; Vaysse, P. J.-J.; He, C.; Branchek, T. A.; Weinshank, R. L. : Expression cloning and pharmacological characterization of a human hippocampal neuropeptide Y/peptide YY Y2 receptor subtype. J. Biol. Chem. 270: 26758–26761, 1995. ; and

[16659] Rose, P. M.; Fernandes, P.; Lynch, J. S.; Frazier, S. T.; Fisher, S. M.; Kodukula, K.; Kienzle, B.; Seethala, R. : Cloning and functional expression of a cDNA encoding a human type 2 ne.

[16660] Further studies establishing the function and utilities of NPY2R are found in John Hopkins OMIM database record ID 162642, and in cited publications numbered 3220–322 and 3218 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187) is another VGAM309 host target gene. OAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OAS3, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OAS3 BINDING SITE, designated SEQ ID:12860, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16661] Another function of VGAM309 is therefore inhibition of 2'-5'-oligoadenylate Synthetase 3, 100kDa (OAS3, Accession NM_006187), a gene which may play a role in mediating resistance to virus infection, control of cell growth, differentiation, and apoptosis. Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OAS3. The function of OAS3 has been established by previous studies. The 2-prime,5-prime oligoadenylate synthetases (OASs) are interferon-induced proteins characterized by their capacity to catalyze the synthesis of 2-prime,5-prime oligomers of adenosine (2-5As). See OAS1 (OMIM Ref. No. 164350). Hovanessian et al. (1987) found that interferon-treated human cells contain several OASs corresponding to proteins of 40 (OAS1), 46 (OAS1), 69 (OAS2; 603350), and 100 kD. Hovnanian et al. (1998) reported that the predicted OAS3, or p100, protein contains 3 adjacent OAS1-like domains. The domains share

44 to 60% protein sequence similarity with each other and 42 to 60% sequence identity with the conserved domain of OAS1. The authors noted that OAS1, OAS2, and OAS3 contain 1, 2, and 3 conserved OAS domains or units, respectively. Northern blot analysis revealed that OAS3 is expressed as a 7-kb interferon-induced mRNA in HeLa cells. By fluorescence in situ hybridization and by inclusion within mapped clones, Hovnanian et al. (1998) determined that the OAS1, OAS2, and OAS3 genes are clustered with a 130-kb region on 12q24.2.

[16662] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16663] Hovanessian, A. G.; Laurent, A. G.; Chebath, J.; Galabru, J.; Robert, N.; Svab, J. : Identification of 69-kd and 100-kd forms of 2-5A synthetase in interferon-treated human cells by specific monoclonal antibodies. EMBO J. 6: 1273-1280, 1987. ; and

[16664] Hovnanian, A.; Rebouillat, D.; Mattei, M.-G.; Levy, E. R.; Marie, I.; Monaco, A. P.; Hovanessian, A. G. : The human 2-prime,5-prime-oligoadenylate synthetase locus is composed of three.

[16665] Further studies establishing the function and utilities of

OAS3 are found in John Hopkins OMIM database record ID 603351, and in cited publications numbered 8009 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. DKFZP564O1664 (Accession NM_030800) is another VGAM309 host target gene. DKFZP564O1664 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O1664, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O1664 BINDING SITE, designated SEQ ID:25102, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16666] Another function of VGAM309 is therefore inhibition of DKFZP564O1664 (Accession NM_030800). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O1664. FLJ12800 (Accession NM_022903) is another VGAM309 host target gene. FLJ12800 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12800, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12800 BINDING SITE, designated SEQ ID:23194, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16667] Another function of VGAM309 is therefore inhibition of FLJ12800 (Accession NM_022903). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12800. FLJ21459 (Accession NM_024521) is another VGAM309 host target gene. FLJ21459 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21459, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21459 BINDING SITE, designated SEQ ID:23720, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16668] Another function of VGAM309 is therefore inhibition of FLJ21459 (Accession NM_024521). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21459.

KIAA0329 (Accession NM_014844) is another VGAM309 host target gene. KIAA0329 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0329, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0329 BINDING SITE, designated SEQ ID:16878, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16669] Another function of VGAM309 is therefore inhibition of KIAA0329 (Accession NM_014844). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0329. KIAA1416 (Accession XM_098762) is another VGAM309 host target gene. KIAA1416 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1416, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1416 BINDING SITE, designated SEQ ID:41806, to the nucleotide sequence of VGAM309 RNA, herein designated

VGAM RNA, also designated SEQ ID:3020.

[16670] Another function of VGAM309 is therefore inhibition of KIAA1416 (Accession XM_098762). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1416. SDF1 (Accession XM_165565) is another VGAM309 host target gene. SDF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SDF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SDF1 BINDING SITE, designated SEQ ID:43688, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16671] Another function of VGAM309 is therefore inhibition of SDF1 (Accession XM_165565). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDF1. LOC146667 (Accession XM_097044) is another VGAM309 host target gene. LOC146667 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146667, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146667 BINDING SITE, designated SEQ ID:40711, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16672] Another function of VGAM309 is therefore inhibition of LOC146667 (Accession XM_097044). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146667. LOC153937 (Accession XM_087813) is another VGAM309 host target gene. LOC153937 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39446, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16673] Another function of VGAM309 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC153937. LOC254057 (Accession XM_173085) is another VGAM309 host target gene. LOC254057 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC254057, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254057 BINDING SITE, designated SEQ ID:46346, to the nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16674] Another function of VGAM309 is therefore inhibition of LOC254057 (Accession XM_173085). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254057. LOC91050 (Accession XM_035703) is another VGAM309 host target gene. LOC91050 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91050, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91050 BINDING SITE, designated SEQ ID:32336, to the

nucleotide sequence of VGAM309 RNA, herein designated VGAM RNA, also designated SEQ ID:3020.

[16675] Another function of VGAM309 is therefore inhibition of LOC91050 (Accession XM_035703). Accordingly, utilities of VGAM309 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91050. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 310 (VGAM310) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16676] VGAM310 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM310 was detected is described hereinabove with reference to Figs. 1–8.

[16677] VGAM310 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pothos Latent Virus. VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16678] VGAM310 gene encodes a VGAM310 precursor RNA,

herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM310 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM310 precursor RNA is designated SEQ ID:296, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:296 is located at position 512 relative to the genome of Pothos Latent Virus.

[16679] VGAM310 precursor RNA folds onto itself, forming VGAM310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16680] An enzyme complex designated DICER COMPLEX, `dices` the VGAM310 folded precursor RNA into VGAM310 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short

~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM310 RNA is designated SEQ ID:3021, and is provided hereinbelow with reference to the sequence listing part.

[16681] VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM310 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16682] VGAM310 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM310 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding

sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM310 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16683] The complementary binding of VGAM310 RNA, herein designated VGAM RNA, to host target binding sites on VGAM310 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM310 host target RNA into VGAM310 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16684] It is appreciated that VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents

a plurality of VGAM310 host target genes. The mRNA of each one of this plurality of VGAM310 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM310 RNA, herein designated VGAM RNA, and which when bound by VGAM310 RNA causes inhibition of translation of respective one or more VGAM310 host target proteins.

[16685] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM310 gene, herein designated VGAM GENE, on one or more VGAM310 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G.,

`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[16686] It is yet further appreciated that a function of VGAM310 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of viral infection by Pothos Latent Virus. Specific functions, and accordingly utilities, of VGAM310 correlate with, and may be deduced from, the identity of the host target genes which VGAM310 binds and inhibits, and the function of these host target genes, as elaborated herein–below.

[16687] Nucleotide sequences of the VGAM310 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM310 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM310 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM310 are further described hereinbelow with reference to Table 1.

[16688] Nucleotide sequences of host target binding sites, such as BINDING SITE–I, BINDING SITE–II and BINDING SITE–III of Fig. 1, found on VGAM310 host target RNA, and schematic representation of the complementarity of each of these

host target binding sites to VGAM310 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16689] As mentioned hereinabove with reference to Fig. 1, a function of VGAM310 gene, herein designated VGAM is inhibition of expression of VGAM310 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM310 correlate with, and may be deduced from, the identity of the target genes which VGAM310 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16690] Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession NM_002224) is a VGAM310 host target gene. ITPR3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITPR3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITPR3 BINDING SITE, designated SEQ ID:7996, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16691] A function of VGAM310 is therefore inhibition of Inositol 1,4,5-triphosphate Receptor, Type 3 (ITPR3, Accession

NM_002224), a gene which may be responsible for calcium release from intracellular stores. Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITPR3. The function of ITPR3 has been established by previous studies. See 147265. Ozcelik et al. (1991) found that a cDNA probe for ITPR3 hybridized to DNA from hybrid cells containing human chromosome 6. In one hybrid that carried 6pter-p21, in the absence of an intact copy of this chromosome, hybridization was observed, thus mapping the gene to 6pter-p21. ITPR3 transduces many hormonal signals that regulate $\text{Ca}(2+)$ -dependent processes in the intestinal epithelium. Maranto (1994) described complete sequence of the ITPR3 polypeptide (2,671 amino acids). Primary structure analysis indicated a pattern of conserved and variable regions, characteristic of the particular gene family. Immunocytochemical localization in the intestine was determined. Yamamoto-Hino et al. (1994) likewise mapped the ITPR3 gene to chromosome 6, specifically to 6p21, by isotopic in situ hybridization. They showed that the type 3 receptor was present in all hematopoietic and lymphoma cell lines tested

[16692] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

[16693] Maranto, A. R. : Primary structure, ligand binding, and localization of the human type 3 inositol

1,4,5-trisphosphate receptor expressed in intestinal epithelium. J. Biol. Chem. 269: 1222-1230, 1994. ; and

[16694] Ozcelik, T.; Suedhof, T. C.; Francke, U. : The genes for inositol 1,4,5-triphosphate receptors 1 (ITPR1) and 3 (ITPR3) are localized on human chromosomes 3p and 6pter-p21, respectively.

[16695] Further studies establishing the function and utilities of ITPR3 are found in John Hopkins OMIM database record ID 147267, and in cited publications numbered 4821-4823 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer-

ence. Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM_014268) is another VGAM310 host target gene. MAPRE2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE2 BINDING

SITE, designated SEQ ID:15547, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16696] Another function of VGAM310 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 2 (MAPRE2, Accession NM_014268), a gene which The functional inactivation of the APC gene product is a key event in colorectal tumorigenesis. Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE2. The function of MAPRE2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM178. Ribosomal Protein L15 (RPL15, Accession NM_002948) is another VGAM310 host target gene. RPL15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPL15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RPL15 BINDING SITE, designated SEQ ID:8859, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16697] Another function of VGAM310 is therefore inhibition of Ribosomal Protein L15 (RPL15, Accession NM_002948). Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPL15. FLJ10737 (Accession NM_018198) is another VGAM310 host target gene. FLJ10737 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10737, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10737 BINDING SITE, designated SEQ ID:20065, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16698] Another function of VGAM310 is therefore inhibition of FLJ10737 (Accession NM_018198). Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10737. Hyaluronan Binding Protein 2 (HABP2, Accession NM_004132) is another VGAM310 host target gene. HABP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HABP2, corresponding to a HOST TARGET binding site such as

BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HABP2 BINDING SITE, designated SEQ ID:10343, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16699] Another function of VGAM310 is therefore inhibition of Hyaluronan Binding Protein 2 (HABP2, Accession NM_004132). Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HABP2. KIAA0553 (Accession XM_045981) is another VGAM310 host target gene. KIAA0553 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0553, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0553 BINDING SITE, designated SEQ ID:34637, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16700] Another function of VGAM310 is therefore inhibition of KIAA0553 (Accession XM_045981). Accordingly, utilities

of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0553. LOC221839 (Accession XM_166506) is another VGAM310 host target gene. LOC221839 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC221839, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221839 BINDING SITE, designated SEQ ID:44432, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16701] Another function of VGAM310 is therefore inhibition of LOC221839 (Accession XM_166506). Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221839. LOC92305 (Accession NM_138385) is another VGAM310 host target gene. LOC92305 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC92305, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

LOC92305 BINDING SITE, designated SEQ ID:28758, to the nucleotide sequence of VGAM310 RNA, herein designated VGAM RNA, also designated SEQ ID:3021.

[16702] Another function of VGAM310 is therefore inhibition of LOC92305 (Accession NM_138385). Accordingly, utilities of VGAM310 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92305. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 311 (VGAM311) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16703] VGAM311 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM311 was detected is described hereinabove with reference to Figs. 1–8.

[16704] VGAM311 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pothos Latent Virus. VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16705] VGAM311 gene encodes a VGAM311 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM311 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM311 precursor RNA is designated SEQ ID:297, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:297 is located at position 2180 relative to the genome of Pothos Latent Virus.

[16706] VGAM311 precursor RNA folds onto itself, forming VGAM311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16707] An enzyme complex designated DICER COMPLEX, `dices` the VGAM311 folded precursor RNA into VGAM311 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a

hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 61%) nucleotide sequence of VGAM311 RNA is designated SEQ ID:3022, and is provided hereinbelow with reference to the sequence listing part.

[16708] VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM311 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16709] VGAM311 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM311 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an il-

illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM311 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[16710] The complementary binding of VGAM311 RNA, herein designated VGAM RNA, to host target binding sites on VGAM311 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM311 host target RNA into VGAM311 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16711] It is appreciated that VGAM311 host target gene, herein

designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM311 host target genes. The mRNA of each one of this plurality of VGAM311 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM311 RNA, herein designated VGAM RNA, and which when bound by VGAM311 RNA causes inhibition of translation of respective one or more VGAM311 host target proteins.

[16712] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM311 gene, herein designated VGAM GENE, on one or more VGAM311 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these

other miRNA genes have not yet been found (Ruvkun G.,
`Perspective: Glimpses of a tiny RNA world`, Science
294,779 (2001)).

[16713] It is yet further appreciated that a function of VGAM311 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of viral infection by Pothos Latent Virus. Specific functions, and accordingly utilities, of VGAM311 correlate with, and may be deduced from, the identity of the host target genes which VGAM311 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16714] Nucleotide sequences of the VGAM311 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM311 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM311 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM311 are further described hereinbelow with reference to Table 1.

[16715] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM311 host target RNA, and schematic

representation of the complementarity of each of these host target binding sites to VGAM311 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16716] As mentioned hereinabove with reference to Fig. 1, a function of VGAM311 gene, herein designated VGAM is inhibition of expression of VGAM311 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM311 correlate with, and may be deduced from, the identity of the target genes which VGAM311 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16717] FLJ20276 (Accession NM_017738) is a VGAM311 host target gene. FLJ20276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20276 BINDING SITE, designated SEQ ID:19329, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16718] A function of VGAM311 is therefore inhibition of FLJ20276

(Accession NM_017738). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20276. MIG (Accession NM_002416) is another VGAM311 host target gene. MIG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MIG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MIG BINDING SITE, designated SEQ ID:8246, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16719] Another function of VGAM311 is therefore inhibition of MIG (Accession NM_002416). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MIG. PLPL (Accession NM_020181) is another VGAM311 host target gene. PLPL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLPL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLPL BINDING SITE, designated SEQ ID:21398,

to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16720] Another function of VGAM311 is therefore inhibition of PLPL (Accession NM_020181). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLPL. Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM_022978) is another VGAM311 host target gene. SERF1B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SERF1B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SERF1B BINDING SITE, designated SEQ ID:23257, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16721] Another function of VGAM311 is therefore inhibition of Small EDRK-rich Factor 1B (centromeric) (SERF1B, Accession NM_022978). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SERF1B. Wingless-type MMTV Integration Site Family, Member 2B (WNT2B, Acces-

sion NM_024494) is another VGAM311 host target gene. WNT2B BINDING SITE1 and WNT2B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT2B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT2B BINDING SITE1 and WNT2B BINDING SITE2, designated SEQ ID:23695 and SEQ ID:10394 respectively, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16722] Another function of VGAM311 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 2B (WNT2B, Accession NM_024494). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT2B. LOC203292 (Accession XM_117527) is another VGAM311 host target gene. LOC203292 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203292, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203292 BINDING

SITE, designated SEQ ID:43502, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16723] Another function of VGAM311 is therefore inhibition of LOC203292 (Accession XM_117527). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203292. LOC91813 (Accession XM_040862) is another VGAM311 host target gene. LOC91813 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91813 BINDING SITE, designated SEQ ID:33397, to the nucleotide sequence of VGAM311 RNA, herein designated VGAM RNA, also designated SEQ ID:3022.

[16724] Another function of VGAM311 is therefore inhibition of LOC91813 (Accession XM_040862). Accordingly, utilities of VGAM311 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91813. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 312 (VGAM312) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16725] VGAM312 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM312 was detected is described hereinabove with reference to Figs. 1–8.

[16726] VGAM312 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Pothos Latent Virus. VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16727] VGAM312 gene encodes a VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM312 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM312 precursor RNA is designated SEQ ID:298, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:298 is located at position 791 relative to the genome of Pothos

Latent Virus.

[16728] VGAM312 precursor RNA folds onto itself, forming VGAM312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16729] An enzyme complex designated DICER COMPLEX, `dices` the VGAM312 folded precursor RNA into VGAM312 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 44%) nucleotide sequence of VGAM312 RNA is designated SEQ ID:3023, and is provided hereinbelow with reference to the sequence listing part.

[16730] VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM312 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16731] VGAM312 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM312 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM312 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16732] The complementary binding of VGAM312 RNA, herein designated VGAM RNA, to host target binding sites on VGAM312 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM312 host target RNA into VGAM312 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16733] It is appreciated that VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM312 host target genes. The mRNA of each one of this plurality of VGAM312 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM312 RNA, herein designated VGAM RNA, and which when bound by VGAM312 RNA causes inhibition of translation of respective one or more VGAM312 host target proteins.

[16734] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM312 gene, herein designated VGAM GENE, on one or more VGAM312 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16735] It is yet further appreciated that a function of VGAM312 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM312 include diagnosis, prevention and treatment of viral infection by Pothos Latent Virus. Specific functions, and accordingly utilities, of VGAM312 correlate

with, and may be deduced from, the identity of the host target genes which VGAM312 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16736] Nucleotide sequences of the VGAM312 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM312 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM312 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM312 are further described hereinbelow with reference to Table 1.

[16737] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM312 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM312 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16738] As mentioned hereinabove with reference to Fig. 1, a function of VGAM312 gene, herein designated VGAM is inhibition of expression of VGAM312 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM312 correlate with, and may be deduced

from, the identity of the target genes which VGAM312 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16739] D8S2298E (Accession NM_005671) is a VGAM312 host target gene. D8S2298E BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by D8S2298E, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of D8S2298E BINDING SITE, designated SEQ ID:12230, to the nucleotide sequence of VGAM312 RNA, herein designated VGAM RNA, also designated SEQ ID:3023.

[16740] A function of VGAM312 is therefore inhibition of D8S2298E (Accession NM_005671). Accordingly, utilities of VGAM312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with D8S2298E. LOC149182 (Accession XM_097605) is another VGAM312 host target gene. LOC149182 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149182, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LOC149182 BINDING SITE, designated SEQ ID:40968, to the nucleotide sequence of VGAM312 RNA, herein designated VGAM RNA, also designated SEQ ID:3023.

[16741] Another function of VGAM312 is therefore inhibition of LOC149182 (Accession XM_097605). Accordingly, utilities of VGAM312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149182. LOC51301 (Accession NM_016591) is another VGAM312 host target gene. LOC51301 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC51301, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51301 BINDING SITE, designated SEQ ID:18673, to the nucleotide sequence of VGAM312 RNA, herein designated VGAM RNA, also designated SEQ ID:3023.

[16742] Another function of VGAM312 is therefore inhibition of LOC51301 (Accession NM_016591). Accordingly, utilities of VGAM312 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51301. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 313 (VGAM313) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16743] VGAM313 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM313 was detected is described hereinabove with reference to Figs. 1–8.

[16744] VGAM313 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Porcine Enteric Calicivirus. VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16745] VGAM313 gene encodes a VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM313 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM313 precursor RNA is designated SEQ ID:299, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:299 is

located at position 2578 relative to the genome of Porcine Enteric Calicivirus.

[16746] VGAM313 precursor RNA folds onto itself, forming VGAM313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16747] An enzyme complex designated DICER COMPLEX, `dices` the VGAM313 folded precursor RNA into VGAM313 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 78%) nucleotide sequence of VGAM313 RNA is designated SEQ ID:3024, and is provided hereinbelow with reference to the sequence listing part.

[16748] VGAM313 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM313 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16749] VGAM313 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM313 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM313 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM313 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[16750] The complementary binding of VGAM313 RNA, herein designated VGAM RNA, to host target binding sites on VGAM313 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM313 host target RNA into VGAM313 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16751] It is appreciated that VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM313 host target genes. The mRNA of each one of this plurality of VGAM313 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM313 RNA, herein designated VGAM RNA, and which when bound by VGAM313 RNA causes inhibition of translation of respective one or more VGAM313

host target proteins.

[16752] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM313 gene, herein designated VGAM GENE, on one or more VGAM313 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16753] It is yet further appreciated that a function of VGAM313 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of viral infection by Porcine Enteric Calicivirus.

Specific functions, and accordingly utilities, of VGAM313 correlate with, and may be deduced from, the identity of the host target genes which VGAM313 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16754] Nucleotide sequences of the VGAM313 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM313 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM313 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM313 are further described hereinbelow with reference to Table 1.

[16755] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM313 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM313 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16756] As mentioned hereinabove with reference to Fig. 1, a function of VGAM313 gene, herein designated VGAM is inhibition of expression of VGAM313 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM313 correlate with, and may be deduced from, the identity of the target genes which VGAM313 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16757] PIAS3 (Accession NM_006099) is a VGAM313 host target gene. PIAS3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIAS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIAS3 BINDING SITE, designated SEQ ID:12744, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16758] A function of VGAM313 is therefore inhibition of PIAS3 (Accession NM_006099), a gene which specifically inhibits activated stat3 signaling by blocking its dna-binding activity. Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIAS3. The function of PIAS3 has been established by previous studies. STAT proteins (e.g., STAT1, 600555) are latent cytoplasmic transcription factors that become activated by tyrosine phosphorylation in response to cytokine stimulation. Using PIAS1 (OMIM Ref.

No. 603566), an inhibitor of activated STAT1, for EST database searches and cDNA library screening, Chung et al. (1997) identified PIAS3, an inhibitor of activated STAT3 (OMIM Ref. No. 102582). They found that PIAS3 has a molecular mass of about 68 kD. Ueki et al. (1999) independently isolated a PIAS3 cDNA encoding a deduced 619-amino acid protein that shares 83% sequence identity with mouse Pias3. PIAS3 also shares approximately 55% identity with PIAS1 and the PIASX proteins (OMIM Ref. No. 603567) and 39% identity with PIASY (OMIM Ref. No. 605989). Northern blot analysis detected wide expression of PIAS3 in human tissues Ueki et al. (1999) identified PIAS3 as an inhibitor of activated STAT3. Levy et al. (2002) found that PIAS3 binds microphthalmia-associated transcription factor (MITF; 156845), a key DNA-binding protein, in rat basophilic leukemia cells and mouse melanocytes. They observed direct binding of MITF by PIAS3 in coimmunoprecipitation and in vitro pull-down assays. Gel-shift assays showed that PIAS3 can block MITF DNA-binding activity, and cotransfection of MITF and PIAS3 in NIH 3T3 cells inhibited MITF-driven transcription activity. Interaction between PIAS3 and MITF was independent of STAT3 binding

- [16759] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:
- [16760] Chung, C. D.; Liao, J.; Liu, B.; Rao, X.; Jay, P.; Berta, P.; Shuai, K. : Specific inhibition of Stat3 signal transduction by PIAS3. *Science* 278: 1803–1805, 1997. ; and
- [16761] Ueki, N.; Seki, N.; Yano, K.; Saito, T.; Masuho, Y.; Muramatsu, M. : Isolation and chromosomal assignment of a human gene encoding protein inhibitor of activated STAT3 (PIAS3). *J. Hum. Gene.*
- [16762] Further studies establishing the function and utilities of PIAS3 are found in John Hopkins OMIM database record ID 605987, and in cited publications numbered 234 and 4110–4111 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference.
- Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749) is another VGAM313 host target gene. C20orf139 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by C20orf139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf139 BINDING

SITE, designated SEQ ID:41106, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16763] Another function of VGAM313 is therefore inhibition of Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf139.

FLJ13322 (Accession NM_024722) is another VGAM313 host target gene. FLJ13322 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ13322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13322 BINDING SITE, designated SEQ ID:24060, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16764] Another function of VGAM313 is therefore inhibition of FLJ13322 (Accession NM_024722). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13322. KIAA0293 (Accession XM_027045) is another VGAM313

host target gene. KIAA0293 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0293, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0293 BINDING SITE, designated SEQ ID:30395, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16765] Another function of VGAM313 is therefore inhibition of KIAA0293 (Accession XM_027045). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0293. Neuropilin (NRP) and Tolloid (TLL)-like 1 (NETO1, Accession NM_138966) is another VGAM313 host target gene. NETO1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by NETO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NETO1 BINDING SITE, designated SEQ ID:29069, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ

ID:3024.

[16766] Another function of VGAM313 is therefore inhibition of Neuropilin (NRP) and Tolloid (TLL)-like 1 (NETO1, Accession NM_138966). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NETO1. LOC147229 (Accession XM_085742) is another VGAM313 host target gene. LOC147229 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC147229, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147229 BINDING SITE, designated SEQ ID:38315, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16767] Another function of VGAM313 is therefore inhibition of LOC147229 (Accession XM_085742). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147229. LOC149837 (Accession XM_097747) is another VGAM313 host target gene. LOC149837 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC149837, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149837 BINDING SITE, designated SEQ ID:41096, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16768] Another function of VGAM313 is therefore inhibition of LOC149837 (Accession XM_097747). Accordingly, utilities of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149837. LOC154214 (Accession XM_087876) is another VGAM313 host target gene. LOC154214 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC154214, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC154214 BINDING SITE, designated SEQ ID:39467, to the nucleotide sequence of VGAM313 RNA, herein designated VGAM RNA, also designated SEQ ID:3024.

[16769] Another function of VGAM313 is therefore inhibition of LOC154214 (Accession XM_087876). Accordingly, utilities

of VGAM313 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC154214. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 314 (VGAM314) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16770] VGAM314 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM314 was detected is described hereinabove with reference to Figs. 1–8.

[16771] VGAM314 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Murine Adenovirus A. VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16772] VGAM314 gene encodes a VGAM314 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM314 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM314 precursor RNA is designated SEQ ID:300, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:300 is located at position 20841 relative to the genome of Murine Adenovirus A.

[16773] VGAM314 precursor RNA folds onto itself, forming VGAM314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16774] An enzyme complex designated DICER COMPLEX, `dices` the VGAM314 folded precursor RNA into VGAM314 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM314 RNA is designated SEQ ID:3025, and

is provided hereinbelow with reference to the sequence listing part.

[16775] VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM314 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16776] VGAM314 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM314 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM314 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16777] The complementary binding of VGAM314 RNA, herein designated VGAM RNA, to host target binding sites on VGAM314 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM314 host target RNA into VGAM314 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16778] It is appreciated that VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM314 host target genes. The mRNA of each one of this plurality of VGAM314 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM314 RNA, herein designated VGAM RNA, and which when bound by VGAM314 RNA causes inhibition of translation of respective one or more VGAM314 host target proteins.

[16779] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM314 gene, herein designated VGAM GENE, on one or more VGAM314 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16780] It is yet further appreciated that a function of VGAM314 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of viral infection by Murine Adenovirus A. Specific functions, and accordingly utilities, of VGAM314 correlate with, and may be deduced from, the identity of the host target genes which VGAM314 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16781] Nucleotide sequences of the VGAM314 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM314 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM314 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM314 are further described hereinbelow with reference to Table 1.

[16782] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM314 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM314 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16783] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM314 gene, herein designated VGAM is inhibition of expression of VGAM314 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM314 correlate with, and may be deduced from, the identity of the target genes which VGAM314 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16784] Male-specific Lethal 3-like 1 (Drosophila) (MSL3L1, Accession NM_006800) is a VGAM314 host target gene. MSL3L1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MSL3L1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MSL3L1 BINDING SITE, designated SEQ ID:13671, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16785] A function of VGAM314 is therefore inhibition of Male-specific Lethal 3-like 1 (Drosophila) (MSL3L1, Accession NM_006800). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MSL3L1. Metal-regulatory

Transcription Factor 1 (MTF1, Accession NM_005955) is another VGAM314 host target gene. MTF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MTF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MTF1 BINDING SITE, designated SEQ ID:12581, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16786] Another function of VGAM314 is therefore inhibition of Metal-regulatory Transcription Factor 1 (MTF1, Accession NM_005955). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MTF1. Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063) is another VGAM314 host target gene. SCD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCD BINDING SITE, designated SEQ ID:11490, to the nucleotide se-

quence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16787] Another function of VGAM314 is therefore inhibition of Stearoyl-CoA Desaturase (delta-9-desaturase) (SCD, Accession NM_005063), a gene which functions in the synthesis of unsaturated fatty acids. Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCD. The function of SCD has been established by previous studies. Stearoyl-CoA desaturase (SCD; EC 1.14.99.5) is an iron-containing enzyme that catalyzes a rate-limiting step in the synthesis of unsaturated fatty acids. The principal product of SCD is oleic acid, which is formed by desaturation of stearic acid. The ratio of stearic acid to oleic acid has been implicated in the regulation of cell growth and differentiation through effects on cell-membrane fluidity and signal transduction (Zhang et al. (1999)). Thiede et al. (1986) isolated cDNAs encoding rat SCD. By RT-PCR of adipose tissue RNA with primers based on the sequence of rat SCD, Li et al. (1994) isolated a partial human SCD cDNA. Using RNase protection assays, the authors found that human SCD was expressed at higher levels in colon and esophageal carcinomas than in the counterpart nor-

mal tissues. Animal model experiments lend further support to the function of SCD. SCD is a central lipogenic enzyme catalyzing the synthesis of monounsaturated fatty acids, mainly oleate (C18:1) and palmitoleate (C16:1), which are components of membrane phospholipids, triglycerides, wax esters, and cholesterol esters. Several SCD isoforms (SCD1, -2, and -3) exist in the mouse. Ntambi et al. (2002) showed that mice with a targeted disruption of the SCD1 isoform had reduced body adiposity, increased insulin (OMIM Ref. No. 176730) sensitivity, and resistance to diet-induced weight gain. The protection from obesity involved increased energy expenditure and increased oxygen consumption. Compared with wild-type mice, the SCD1-/- mice had increased levels of plasma ketone bodies but reduced levels of plasma insulin and leptin. In these homozygous null mice, the expression of several genes of lipid oxidation was upregulated, whereas lipid synthesis genes were downregulated. These observations suggested that a consequence of SCD1 deficiency is an activation of lipid oxidation in addition to reduced triglyceride synthesis and storage.

[16788] It is appreciated that the abovementioned animal model for SCD is acknowledged by those skilled in the art as a

scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[16789] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16790] Ntambi, J. M.; Miyazaki, M.; Stoeckl, J. P.; Lan, H.; Kendziora, C. M.; Yandell, B. S.; Song, Y.; Cohen, P.; Friedman, J. M.; Attie, A. D. : Loss of stearoyl-CoA desaturase-1 function protects mice against adiposity. Proc. Nat. Acad. Sci. 99: 11482–11486, 2002. ; and

[16791] Zhang, L.; Ge, L.; Parimoo, S.; Stenn, K.; Prouty, S. M. : Human stearoyl-CoA desaturase: alternative transcripts generated from a single gene by usage of tandem polyadenylation sites.

[16792] Further studies establishing the function and utilities of SCD are found in John Hopkins OMIM database record ID 604031, and in cited publications numbered 317 and 7635–7639 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 26, Member 3 (SLC26A3, Accession NM_000111) is another VGAM314 host target gene. SLC26A3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by

SLC26A3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC26A3 BINDING SITE, designated SEQ ID:5576, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16793] Another function of VGAM314 is therefore inhibition of Solute Carrier Family 26, Member 3 (SLC26A3, Accession NM_000111). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC26A3. Staufen, RNA Binding Protein, Homolog 2 (Drosophila) (STAU2, Accession NM_014393) is another VGAM314 host target gene. STAU2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STAU2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAU2 BINDING SITE, designated SEQ ID:15722, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16794] Another function of VGAM314 is therefore inhibition of Staufen, RNA Binding Protein, Homolog 2 (Drosophila) (STAU2, Accession NM_014393). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAU2. Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662) is another VGAM314 host target gene. TRPM6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRPM6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRPM6 BINDING SITE, designated SEQ ID:19201, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16795] Another function of VGAM314 is therefore inhibition of Transient Receptor Potential Cation Channel, Subfamily M, Member 6 (TRPM6, Accession NM_017662), a gene which contains a predicted ion channel domain and a protein kinase domain. Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRPM6. The function of

TRPM6 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM173.DKFZP564O0423 (Accession XM_166254) is another VGAM314 host target gene. DKFZP564O0423 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564O0423, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564O0423 BINDING SITE, designated SEQ ID:44064, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16796] Another function of VGAM314 is therefore inhibition of DKFZP564O0423 (Accession XM_166254). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564O0423. FLJ10688 (Accession NM_018179) is another VGAM314 host target gene. FLJ10688 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10688, corresponding to a HOST TARGET binding site such as BINDING

SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10688 BINDING SITE, designated SEQ ID:20013, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16797] Another function of VGAM314 is therefore inhibition of FLJ10688 (Accession NM_018179). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10688. FLJ12960 (Accession NM_024638) is another VGAM314 host target gene. FLJ12960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE, designated SEQ ID:23917, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16798] Another function of VGAM314 is therefore inhibition of FLJ12960 (Accession NM_024638). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12960.

KIAA1668 (Accession XM_039236) is another VGAM314 host target gene. KIAA1668 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1668, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1668 BINDING SITE, designated SEQ ID:33027, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16799] Another function of VGAM314 is therefore inhibition of KIAA1668 (Accession XM_039236). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1668. MAD4 (Accession NM_006454) is another VGAM314 host target gene. MAD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAD4 BINDING SITE, designated SEQ ID:13171, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3025.

[16800] Another function of VGAM314 is therefore inhibition of MAD4 (Accession NM_006454). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAD4. MGC4643 (Accession NM_032715) is another VGAM314 host target gene. MGC4643 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC4643, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC4643 BINDING SITE, designated SEQ ID:26440, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16801] Another function of VGAM314 is therefore inhibition of MGC4643 (Accession NM_032715). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC4643. WIRE (Accession XM_085731) is another VGAM314 host target gene. WIRE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WIRE, corresponding to a HOST TAR-

GET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WIRE BINDING SITE, designated SEQ ID:38314, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16802] Another function of VGAM314 is therefore inhibition of WIRE (Accession XM_085731). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WIRE. LOC125988 (Accession XM_058957) is another VGAM314 host target gene. LOC125988 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC125988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC125988 BINDING SITE, designated SEQ ID:36803, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16803] Another function of VGAM314 is therefore inhibition of LOC125988 (Accession XM_058957). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC125988. LOC143451 (Accession XM_084521) is another VGAM314 host target gene. LOC143451 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC143451, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143451 BINDING SITE, designated SEQ ID:37621, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16804] Another function of VGAM314 is therefore inhibition of LOC143451 (Accession XM_084521). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143451. LOC145125 (Accession XM_085025) is another VGAM314 host target gene. LOC145125 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145125, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145125 BINDING SITE, designated SEQ ID:37798, to

the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16805] Another function of VGAM314 is therefore inhibition of LOC145125 (Accession XM_085025). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145125. LOC148109 (Accession XM_086047) is another VGAM314 host target gene. LOC148109 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148109, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148109 BINDING SITE, designated SEQ ID:38463, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16806] Another function of VGAM314 is therefore inhibition of LOC148109 (Accession XM_086047). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148109. LOC148696 (Accession XM_097505) is another VGAM314 host target gene. LOC148696 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC148696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148696 BINDING SITE, designated SEQ ID:40893, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16807] Another function of VGAM314 is therefore inhibition of LOC148696 (Accession XM_097505). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148696. LOC149506 (Accession XM_097661) is another VGAM314 host target gene. LOC149506 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC149506, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149506 BINDING SITE, designated SEQ ID:41009, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16808] Another function of VGAM314 is therefore inhibition of LOC149506 (Accession XM_097661). Accordingly, utilities

of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149506. LOC254440 (Accession XM_173126) is another VGAM314 host target gene. LOC254440 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254440, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254440 BINDING SITE, designated SEQ ID:46375, to the nucleotide sequence of VGAM314 RNA, herein designated VGAM RNA, also designated SEQ ID:3025.

[16809] Another function of VGAM314 is therefore inhibition of LOC254440 (Accession XM_173126). Accordingly, utilities of VGAM314 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254440. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 315 (VGAM315) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16810] VGAM315 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM315 was detected is described hereinabove with reference to Figs. 1–8.

[16811] VGAM315 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 3. VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16812] VGAM315 gene encodes a VGAM315 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM315 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM315 precursor RNA is designated SEQ ID:301, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:301 is located at position 1554 relative to the genome of Cryphonectria Hypovirus 3.

[16813] VGAM315 precursor RNA folds onto itself, forming VGAM315 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this

`hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16814] An enzyme complex designated DICER COMPLEX, `dices` the VGAM315 folded precursor RNA into VGAM315 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 60%) nucleotide sequence of VGAM315 RNA is designated SEQ ID:3026, and is provided hereinbelow with reference to the sequence listing part.

[16815] VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM315 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN

CODING and 3`UTR respectively.

[16816] VGAM315 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM315 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM315 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16817] The complementary binding of VGAM315 RNA, herein designated VGAM RNA, to host target binding sites on VGAM315 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM315 host target RNA into VGAM315 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16818] It is appreciated that VGAM315 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM315 host target genes. The mRNA of each one of this plurality of VGAM315 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM315 RNA, herein designated VGAM RNA, and which when bound by VGAM315 RNA causes inhibition of translation of respective one or more VGAM315 host target proteins.

[16819] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM315 gene, herein designated VGAM GENE, on one or more VGAM315 host target gene, herein designated

VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16820] It is yet further appreciated that a function of VGAM315 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 3. Specific functions, and accordingly utilities, of VGAM315 correlate with, and may be deduced from, the identity of the host target genes which VGAM315 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16821] Nucleotide sequences of the VGAM315 precursor RNA,

herein designated VGAM PRECURSOR RNA, and of the
`diced` VGAM315 RNA, herein designated VGAM RNA,
and a schematic representation of the secondary folding
of VGAM315 folded precursor RNA, herein designated
VGAM FOLDED PRECURSOR RNA, of VGAM315 are further
described hereinbelow with reference to Table 1.

[16822] Nucleotide sequences of host target binding sites, such as
BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of
Fig. 1, found on VGAM315 host target RNA, and schematic
representation of the complementarity of each of these
host target binding sites to VGAM315 RNA, herein desig-
nated VGAM RNA, are described hereinbelow with refer-
ence to Table 2.

[16823] As mentioned hereinabove with reference to Fig. 1, a
function of VGAM315 gene, herein designated VGAM is
inhibition of expression of VGAM315 target genes. It is
appreciated that specific functions, and accordingly utili-
ties, of VGAM315 correlate with, and may be deduced
from, the identity of the target genes which VGAM315
binds and inhibits, and the function of these target genes,
as elaborated hereinbelow.

[16824] G Protein-coupled Receptor, Family C, Group 5, Member B
(GPRC5B, Accession NM_016235) is a VGAM315 host tar-

get gene. GPRC5B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GPRC5B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPRC5B BINDING SITE, designated SEQ ID:18352, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16825] A function of VGAM315 is therefore inhibition of G Protein-coupled Receptor, Family C, Group 5, Member B (GPRC5B, Accession NM_016235), a gene which belongs to G protein-coupled receptor. Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPRC5B. The function of GPRC5B and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM131. Interleukin 20 Receptor, Alpha (IL20RA, Accession NM_014432) is another VGAM315 host target gene. IL20RA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL20RA, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL20RA BINDING SITE, designated SEQ ID:15791, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16826] Another function of VGAM315 is therefore inhibition of Interleukin 20 Receptor, Alpha (IL20RA, Accession NM_014432), a gene which is the receptor for interleukin-20 . Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL20RA. The function of IL20RA has been established by previous studies. Blumberg et al. (2001) identified the receptor for interleukin-20 (IL20; 605619) as a heterodimer of 2 orphan class II cytokine receptor subunits, IL20RA, also called ZCYTOR7, and IL20RB (OMIM Ref. No. 605621), also called DIRS1. Binding assays using radiolabeled ligand demonstrated that IL20 bound to BHK transfectants expressing both IL20RA and IL20RB, but not to untransfected cells nor to transfectants expressing either receptor subunit alone. Binding of (125)I-labeled IL20 was eliminated in the presence of 100-fold excess of unlabeled IL20 but not in the presence

of 100-fold excess of the unrelated cytokine, IL21 (OMIM Ref. No. 605384). The binding data revealed 88,000 IL20 receptors per cell, with a binding affinity of approximately 1.5 nM. Both receptor subunits were expressed in skin and were dramatically upregulated in psoriatic skin. Scott (2001) mapped the IL20RA gene to 6q23 based on sequence similarity between the IL20RA sequence (GenBank AF184971) and a genomic contig (GenBank NT_025741.1).

[16827] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16828] Blumberg, H.; Conklin, D.; Xu, W.; Grossmann, A.; Brender, T.; Carollo, S.; Eagan, M.; Foster, D.; Haldeman, B. A.; Hammond, A.; Haugen, H.; Jelinek, L.; and 14 others : Interleukin 20: discovery, receptor identification, and role in epidermal function. Cell 104: 9–19, 2001. ; and

[16829] Scott, A. F. : Personal Communication. Baltimore, Md., 3/13/2001.

[16830] Further studies establishing the function and utilities of IL20RA are found in John Hopkins OMIM database record ID 605620, and in cited publications numbered 443 and 7005 listed in the bibliography section hereinbelow, which

are also hereby incorporated by reference. Microtubule-associated Protein 1A (MAP1A, Accession NM_002373) is another VGAM315 host target gene. MAP1A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAP1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1A BINDING SITE, designated SEQ ID:8184, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16831] Another function of VGAM315 is therefore inhibition of Microtubule-associated Protein 1A (MAP1A, Accession NM_002373), a gene which is a structural protein involved in the filamentous cross-bridging between microtubules and other skeletal elements. Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1A. The function of MAP1A has been established by previous studies. Ikeda et al. (2002) identified the MAP1A gene as the 'modifier of tubby hearing-1' (moth1) QTL associated with hearing loss in tubby mutants on the C57BL/6J back-

ground. The Map1a cDNA derived from B6 contained 12 single-nucleotide differences which could lead to amino acid alterations and a difference in the length of a repeat in the open reading frame when compared with that found in the AKR strain. Ikeda et al. (2002) used a transgenic rescue experiment to verify that sequence polymorphisms were crucial for hearing loss phenotype and demonstrated that the polymorphisms changed the binding efficiency of MAP1A to PSD95 (OMIM Ref. No. 602887), a core component in the cytoarchitecture of synapses. This indicates that at least some of the observed polymorphisms are functionally important and that the hearing loss of C57BL/6J-tub/tub mice may be caused by impaired protein interactions involving MTAP1A. Lien et al. (1994) completely cloned and sequenced the human MAP1B gene. By comparison of human MAP1B with sequence databases, they identified a MAP1B-related gene that is probably the human homolog of rat MAP1A. The human MAP1A gene is expressed at high levels in brain and spinal cord and at much lower levels in muscle.

[16832] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

- [16833] Ikeda, A.; Zheng, Q. Y.; Zuberi, A. R.; Johnson, K. R.; Nagert, J. K.; Nishina, P. M. : Microtubule-associated protein 1A is a modifier of tubby hearing (moth1). *Nature Genet.* 30: 401–405, 2002. ; and
- [16834] Lien, L. L.; Feener, C. A.; Fischbach, N.; Kunkel, L. M. : Cloning of human microtubule-associated protein 1B and the identification of a related gene on chromosome 15. *Genomics* 22: 273–28.
- [16835] Further studies establishing the function and utilities of MAP1A are found in John Hopkins OMIM database record ID 600178, and in cited publications numbered 8783, 1074 and 10749 listed in the bibliography section herein–below, which are also hereby incorporated by reference. Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896) is another VGAM315 host target gene. VPS26 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by VPS26, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VPS26 BINDING SITE, designated SEQ ID:11326, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16836] Another function of VGAM315 is therefore inhibition of Vacuolar Protein Sorting 26 (yeast) (VPS26, Accession NM_004896), a gene which is a sorting protein– ensures the proper delivery of organelle–specific proteins. Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VPS26. The function of VPS26 has been established by previous studies. Haft et al. (2000) used yeast 2–hybrid assays, mutation analysis, and expression in mammalian cells to define the binding interactions among VPS26 and other human orthologs of yeast vacuolar protein sorting proteins, VPS29 (OMIM Ref. No. 606932), SNX1 (OMIM Ref. No. 601272), and VPS35 (OMIM Ref. No. 606931). Their results are consistent with a model in which VPS26 is bound to VPS35 in a multimeric complex. Haft et al. (2000) identified a discrete domain within VPS35 that interacts with VPS26. Gel filtration chromatography of COS–7 cells showed that both recombinant and endogenous VPS proteins coelute as a 220– to 240–kD complex, and in the absence of VPS35, neither VPS26 nor VPS29 is found in the complex. By database searching with the *S. cerevisiae* and mouse Vps26p/HB58/PEP8 sequences as probe, Haft et al. (2000) identified a human

VPS26 EST. The deduced 327–amino acid protein was predicted to be a soluble protein. Northern blot analysis of multiple human tissues revealed ubiquitous expression of a single transcript of about 3 kb. Highest expression was found in heart, skeletal muscle, kidney, liver, and placenta, with lower expression in brain, spleen, small intestine, and lung, and lowest expression in colon, thymus, and leukocytes.

[16837] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16838] Haft, C. R.; de la Luz Sierra, M.; Bafford, R.; Lesniak, M. A.; Barr, V. A.; Taylor, S. I. : Human orthologs of yeast vacuolar protein sorting proteins Vps26, 29, and 35: assembly into multimeric complexes. *Molec. Biol. Cell* 11: 4105–4116, 2000. ; and

[16839] Mao, M.; Fu, G.; Wu, J.–S.; Zhang, Q.–H.; Zhou, J.; Kan, L.–X.; Huang, Q.–H.; He, K.–L.; Gu, B.–W.; Han, Z.–G.; Shen, Y.; Gu, J.; Yu, Y.–P.; Xu, S.–H.; Wang, Y.–X.; Chen, S.–J.; Chen.

[16840] Further studies establishing the function and utilities of VPS26 are found in John Hopkins OMIM database record ID 605506, and in cited publications numbered 449 and

8801 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cadherin-like 22 (CDH22, Accession NM_021248) is another VGAM315 host target gene. CDH22 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CDH22, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CDH22 BINDING SITE, designated SEQ ID:22215, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16841] Another function of VGAM315 is therefore inhibition of Cadherin-like 22 (CDH22, Accession NM_021248). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CDH22. LOC124930 (Accession XM_058867) is another VGAM315 host target gene. LOC124930 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC124930, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC124930 BINDING SITE, designated SEQ ID:36769, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16842] Another function of VGAM315 is therefore inhibition of LOC124930 (Accession XM_058867). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124930. LOC130074 (Accession XM_072228) is another VGAM315 host target gene. LOC130074 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC130074, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130074 BINDING SITE, designated SEQ ID:37474, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16843] Another function of VGAM315 is therefore inhibition of LOC130074 (Accession XM_072228). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130074. LOC133584 (Accession XM_059661) is another VGAM315 host target gene. LOC133584 BINDING

SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC133584, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC133584 BINDING SITE, designated SEQ ID:37046, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16844] Another function of VGAM315 is therefore inhibition of LOC133584 (Accession XM_059661). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC133584. LOC145216 (Accession XM_096730) is another VGAM315 host target gene. LOC145216 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145216, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145216 BINDING SITE, designated SEQ ID:40506, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16845] Another function of VGAM315 is therefore inhibition of

LOC145216 (Accession XM_096730). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145216. LOC199232 (Accession XM_114336) is another VGAM315 host target gene. LOC199232 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199232, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199232 BINDING SITE, designated SEQ ID:42880, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16846] Another function of VGAM315 is therefore inhibition of LOC199232 (Accession XM_114336). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199232. LOC200933 (Accession XM_117294) is another VGAM315 host target gene. LOC200933 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200933, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC200933 BINDING SITE, designated SEQ ID:43362, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16847] Another function of VGAM315 is therefore inhibition of LOC200933 (Accession XM_117294). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200933. LOC92249 (Accession XM_043814) is another VGAM315 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92249, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34022, to the nucleotide sequence of VGAM315 RNA, herein designated VGAM RNA, also designated SEQ ID:3026.

[16848] Another function of VGAM315 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM315 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 316 (VGAM316) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16849] VGAM316 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM316 was detected is described hereinabove with reference to Figs. 1–8.

[16850] VGAM316 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 3. VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16851] VGAM316 gene encodes a VGAM316 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM316 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM316 precursor RNA is designated SEQ ID:302, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:302 is

located at position 6108 relative to the genome of Cryphonectria Hypovirus 3.

[16852] VGAM316 precursor RNA folds onto itself, forming VGAM316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16853] An enzyme complex designated DICER COMPLEX, `dices` the VGAM316 folded precursor RNA into VGAM316 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 67%) nucleotide sequence of VGAM316 RNA is designated SEQ ID:3027, and is provided hereinbelow with reference to the sequence listing part.

[16854] VGAM316 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM316 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16855] VGAM316 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM316 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM316 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM316 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[16856] The complementary binding of VGAM316 RNA, herein designated VGAM RNA, to host target binding sites on VGAM316 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM316 host target RNA into VGAM316 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16857] It is appreciated that VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM316 host target genes. The mRNA of each one of this plurality of VGAM316 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM316 RNA, herein designated VGAM RNA, and which when bound by VGAM316 RNA causes inhibition of translation of respective one or more VGAM316

host target proteins.

[16858] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM316 gene, herein designated VGAM GENE, on one or more VGAM316 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16859] It is yet further appreciated that a function of VGAM316 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 3.

Specific functions, and accordingly utilities, of VGAM316 correlate with, and may be deduced from, the identity of the host target genes which VGAM316 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16860] Nucleotide sequences of the VGAM316 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM316 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM316 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM316 are further described hereinbelow with reference to Table 1.

[16861] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM316 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM316 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16862] As mentioned hereinabove with reference to Fig. 1, a function of VGAM316 gene, herein designated VGAM is inhibition of expression of VGAM316 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM316 correlate with, and may be deduced from, the identity of the target genes which VGAM316 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16863] Adaptor-related Protein Complex 1, Gamma 1 Subunit (AP1G1, Accession NM_001128) is a VGAM316 host target gene. AP1G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1G1 BINDING SITE, designated SEQ ID:6800, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16864] A function of VGAM316 is therefore inhibition of Adaptor-related Protein Complex 1, Gamma 1 Subunit (AP1G1, Accession NM_001128), a gene which promotes the formation of clathrin-coated pits and vesicles. Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1G1. The function of AP1G1 has been established by previous studies. Adaptins are important components of

heterotetrameric adaptor complexes (APs) whose role is to promote the formation of clathrin-coated pits and vesicles. The AP-1 adaptor, localized at the trans-Golgi network, is composed of 2 approximately 100-kD subunits, beta-prime-adaptin (OMIM Ref. No. 600157) and gamma-adaptin; 1 medium subunit, AP47 (OMIM Ref. No. 603535); and 1 small subunit, AP19 (OMIM Ref. No. 603531). By screening a human fetal brain library with a mouse gamma-adaptin cDNA, Peyrard et al. (1998) isolated cDNAs encoding human gamma-adaptin. The predicted 825-amino acid protein shares 99% identity with mouse gamma-adaptin. Northern blot analysis revealed that gamma-adaptin was expressed as a 7.5-kb transcript in all human tissues tested. An additional 4.4-kb mRNA was present in most tissues, and an 8.5-kb mRNA was detected in pancreas and peripheral blood leukocytes

[16865] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16866] Doray, B.; Ghosh, P.; Griffith, J.; Geuze, H. J.; Kornfeld, S. : Cooperation of GGAs and AP-1 in packaging MPRs at the trans-Golgi network. Science 297: 1700-1703, 2002. ; and

- [16867] Peyrard, M.; Parveneh, S.; Lagercrantz, S.; Ekman, M.; Fransson, I.; Sahlen, S.; Dumanski, J. P. : Cloning, expression pattern, and chromosomal assignment to 16q23 of the human gamma-a.
- [16868] Further studies establishing the function and utilities of AP1G1 are found in John Hopkins OMIM database record ID 603533, and in cited publications numbered 12596 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Cold Autoinflammatory Syndrome 1 (CIAS1, Accession NM_004895) is another VGAM316 host target gene. CIAS1 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CIAS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CIAS1 BINDING SITE, designated SEQ ID:11321, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.
- [16869] Another function of VGAM316 is therefore inhibition of Cold Autoinflammatory Syndrome 1 (CIAS1, Accession NM_004895), a gene which may mediate protein-protein interactions; contains a leucine rich repeat. Accordingly,

utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CIAS1. The function of CIAS1 has been established by previous studies. In a positional cloning effort to identify the gene mutated in familial cold autoinflammatory syndrome and Muckle-Wells syndrome, both of which map to 1q44, Hoffman et al. (2001) cloned and characterized the CIAS1 gene, so named for 'cold-induced autoinflammatory syndrome.' The full-length cDNA corresponds to a 9-exon gene encoding an open reading frame of 3,105 basepairs with 2 potential start codons in exon 1, with the second start codon meeting more Kozak criteria, and a stop codon at exon 9. Northern blot analysis identified a broad mRNA band of approximately 4 kb expressed at a low level in peripheral blood leukocytes; little or no expression was detectable in other tissues. Further analysis revealed extensive alternative splicing of exons 4 through 8 that resulted in mRNAs ranging from 3,315 to 4,170 bp, consistent with the Northern blot analysis. The predicted protein encoded by the first splice form of CIAS1 (exons 1-3, 5, and 7-9), called cryopyrin, consists of 920 amino acids with a size of 105.7 kD and a PI of 6.16. The protein sequence contains several distinct motifs including a pyrin

domain in the amino terminus (amino acids 13 through 83), a central nucleotide-binding site (NACHT subfamily) domain in exon 3 (amino acids 217 to 533), and a C-terminal leucine-rich repeat domain containing 7 leucine-rich repeats (amino acids 697 through 920). No nuclear localization signals were identified and no clear trans-membrane regions were found. The largest protein potentially encoded by the 9 exons of CIAS1 consists of 1,034 amino acids with a size of 117.9 kD and 11 C-terminal leucine-rich repeats. Hoffman et al. (2001) suggested that cryopyrin is a signaling protein involved in the regulation of apoptosis. Dode et al. (2002) identified CIAS1 mutations, all located in exon 3, in 9 unrelated families with MWS and in 3 unrelated families with familial cold urticaria (FCU), originating from France, England, and Algeria. Five mutations were novel. The R260W mutation (606416.0005) was identified in 2 families with MWS and in 2 families with FCU, of different ethnic origins, thereby demonstrating that a single CIAS1 mutation may cause both syndromes. This result indicated that modifier genes are involved in determining either an MWS or an FCU phenotype. The finding of the G569R mutation (606416.0006) in asymptomatic individuals further em-

phasized the importance of a modifier gene (or genes) in determining disease phenotype. The authors suggested that identification of modifiers was likely to have significant therapeutic implications for these severe diseases.

[16870] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16871] Dode, C.; Le Du, N.; Cuisset, L.; Letourneur, F.; Berthelot, J.-M.; Vaudour, G.; Meyrier, A.; Watts, R. A.; Scott, D. G. I.; Nicholls, A.; Granel, B.; Frances, C.; Garcier, F.; Edery, P.; Boulinguez, S.; Domergues, J.-P.; Delpech, M.; Grateau, G. : New mutations of CIAS1 that are responsible for Muckle-Wells syndrome and familial cold urticaria: a novel mutation underlies both syndromes. *Am. J. Hum. Genet.* 70: 1498–1506, 2002. ; and

[16872] Hoffman, H. M.; Mueller, J. L.; Broide, D. H.; Wanderer, A. A.; Kolodner, R. D. : Mutation of a new gene encoding a putative pyrin-like protein causes familial cold autoinflammatory syn.

[16873] Further studies establishing the function and utilities of CIAS1 are found in John Hopkins OMIM database record ID 606416, and in cited publications numbered 6762–6763, 120 and 8801 listed in the bibliography section hereinbe–

low, which are also hereby incorporated by reference. Coagulation Factor II (thrombin) Receptor (F2R, Accession NM_001992) is another VGAM316 host target gene. F2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by F2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F2R BINDING SITE, designated SEQ ID:7721, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16874] Another function of VGAM316 is therefore inhibition of Coagulation Factor II (thrombin) Receptor (F2R, Accession NM_001992), a gene which Thrombin receptor; G protein-coupled receptor involved in platelet activation. Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F2R. The function of F2R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM140. LIM Domain Kinase 1 (LIMK1, Accession NM_016735) is another VGAM316 host target gene. LIMK1 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by LIMK1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LIMK1 BINDING SITE, designated SEQ ID:18793, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16875] Another function of VGAM316 is therefore inhibition of LIM Domain Kinase 1 (LIMK1, Accession NM_016735). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LIMK1. Microtubule-associated Protein 1B (MAP1B, Accession NM_005909) is another VGAM316 host target gene. MAP1B BINDING SITE1 and MAP1B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by MAP1B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAP1B BINDING SITE1 and MAP1B BINDING SITE2, designated SEQ ID:12535 and SEQ ID:25712 respectively, to the nucleotide sequence of VGAM316 RNA, herein designated

VGAM RNA, also designated SEQ ID:3027.

[16876] Another function of VGAM316 is therefore inhibition of Microtubule-associated Protein 1B (MAP1B, Accession NM_005909), a gene which may have a role in neuronal plasticity and brain development. Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAP1B. The function of MAP1B has been established by previous studies. Using a polyclonal antiserum directed against the C-terminal domain of dystrophin, Lien et al. (1991) isolated a cDNA clone encoding an antigenically crossreactive protein, microtubule-associated protein 1B (MAP1B). By in situ hybridization, the gene was mapped to 5q13 in proximity to the spinal muscular atrophy (SMA; 253300) locus. Genetic linkage analysis of SMA families using a human dinucleotide repeat polymorphism just 3-prime of the MAP1B gene has shown tight linkage to SMA mutations. These mapping data, together with the postulated role of MAP1B in neuronal morphogenesis and its localization in anterior horn motor neurons, suggest a possible association with SMA. The maximum lod score between SMA and MAP1B for combined sexes was 20.24 at a recombination fraction of 0.02. The 2 recombinants between MAP1B and

SMA might appear to eliminate the possibility of an etio-logic relationship between MAP1B and SMA. However, there is likely to be nonallelic heterogeneity, particularly among chronic cases of SMA. If MAP1B were indeed the SMA locus, it would be expected to be recombinant in families that have mutations at another locus. MAP1B was found to be the closest marker distal to the locus for SMA; its 5-prime end was oriented toward the centromere (Wirth et al., 1993). Hammarback et al. (1991) found that LC1, one of the 3 light chains that makes up the MAP1B complex, is encoded within the 3-prime end of the MAP1B heavy chain gene. Their data suggested that the heavy chain and light chain 1 are produced by proteolytic processing of a precursor polypeptide. Lien et al. (1994) completely cloned and sequenced the human MAP1B gene. The expressed protein showed 91% overall identity with rat and mouse MAP1B. The gene has 7 exons; the third exon contains sequence not represented in mouse or rat MAP1B. This sequence, labeled 3A, is present at the 5-prime end of an alternative transcript that is expressed at approximately one-tenth the level of the full-length transcript. Neuronal microtubules are considered to have a role in dendrite and axon formation. Different portions

of the developing and adult brain microtubules are associated with different microtubule-associated proteins. MAP1B is expressed in different portions of the brain and may have a role in neuronal plasticity and brain development. Edelman et al. (1996) generated mice that carry an insertion in MAP1B by gene-targeting methods. Mice homozygous for the modification died during embryogenesis. The heterozygotes exhibited a spectrum of phenotypes including slower growth rates, lack of visual acuity in one or both eyes, and motor system abnormalities. Histochemical analysis of the severely affected mice revealed that their Purkinje cell dendritic processes were abnormal, did not react with MAP1B antibodies, and showed reduced staining with MAP1A (OMIM Ref. No. 600178) antibodies. Similar histologic and immunochemical changes were observed in the olfactory bulb, hippocampus, and retina, providing a basis for the observed phenotypes

[16877] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16878] Lien, L. L.; Feener, C. A.; Fischbach, N.; Kunkel, L. M. : Cloning of human microtubule-associated protein 1B and the identification of a related gene on chromosome 15.

Genomics 22: 273–280, 1994. ; and

[16879] Edelmann, W.; Zervas, M.; Costello, P.; Roback. L.; Fischer, I.; Hammarback, J. A.; Cowan, N.; Davies, P.; Wainer, B.; Kucherlapati, R. : Neuronal abnormalities in microtubule-associated pr.

[16880] Further studies establishing the function and utilities of MAP1B are found in John Hopkins OMIM database record ID 157129, and in cited publications numbered 10746–10751 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Matrix Metalloproteinase 25 (MMP25, Accession NM_022468) is another VGAM316 host target gene. MMP25 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMP25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP25 BINDING SITE, designated SEQ ID:22819, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16881] Another function of VGAM316 is therefore inhibition of Matrix Metalloproteinase 25 (MMP25, Accession

NM_022468). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP25. Myosin IA (MYO1A, Accession NM_005379) is another VGAM316 host target gene. MYO1A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MYO1A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MYO1A BINDING SITE, designated SEQ ID:11861, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16882] Another function of VGAM316 is therefore inhibition of Myosin IA (MYO1A, Accession NM_005379), a gene which is involved in directing the movement of organelles along actin filaments (potential). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MYO1A. The function of MYO1A has been established by previous studies. Myosins are molecular motors that, upon interaction with actin filaments, utilize energy from ATP hydrolysis to generate mechanical force. Phylogenetic analysis of

the myosin motor domains identified 11 distinct classes, 7 of which are expressed in vertebrates (reviewed by Mooseker and Cheney, 1995). These 7 vertebrate myosin classes include conventional myosin (myosin II) and 6 less well characterized unconventional myosin classes, myosins I, V (see OMIM Ref. No. 160777), VI (OMIM Ref. No. 600970), VII (see OMIM Ref. No. 276903), IX, and X (OMIM Ref. No. 601481). Each myosin has a conserved N-terminal motor domain (25 to 40% identical at the amino acid level) that contains both ATP-binding and actin-binding sequences. Following the motor domain is a light-chain-binding 'neck' region containing 1–6 copies of a repeat element, the IQ motif, that serves as a binding site for calmodulin (OMIM Ref. No. 114180) or other members of the EF-hand superfamily of calcium-binding proteins. At the C-terminus, each myosin class has a distinct tail domain that serves in dimerization, membrane binding, protein binding, and/or enzymatic activities and targets each myosin to its particular subcellular location (Hasson et al., 1996). By interspecific mouse backcross mapping, Hasson et al. (1996) localized the Myo1a gene to mouse chromosome 10 which predicted a location of the human homolog on 12q13. By fluorescence in situ hybridization,

they demonstrated that the human MYO1A gene is located on 12q13–q15.

[16883] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[16884] Hasson, T.; Skowron, J. F.; Gilbert, D. J.; Avraham, K. B.; Perry, W. L.; Bement, W. M.; Anderson, B. L.; Sherr, E. H.; Chen, Z.–Y.; Greene, L. A.; Ward, D. C.; Corey, D. P.; Mooseker, M. S.; Copeland, N. G.; Jenkins, N. A. : Mapping of unconventional myosins in mouse and human. *Genomics* 36: 431–439, 1996. ; and

[16885] Mooseker, M. S.; Cheney, R. E. : Unconventional myosins. *Annu. Rev. Cell Dev. Biol.* 11: 633–675, 1995.

[16886] Further studies establishing the function and utilities of MYO1A are found in John Hopkins OMIM database record ID 601478, and in cited publications numbered 7027 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130833) is another VGAM316 host target gene. OPA1 BINDING SITE1 through OPA1 BINDING SITE5 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by OPA1, corresponding to HOST TARGET binding sites such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPA1 BINDING SITE1 through OPA1 BINDING SITE5, designated SEQ ID:28326, SEQ ID:28334, SEQ ID:28342, SEQ ID:28350 and SEQ ID:28358 respectively, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16887] Another function of VGAM316 is therefore inhibition of Optic Atrophy 1 (autosomal dominant) (OPA1, Accession NM_130833). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPA1. Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945) is another VGAM316 host target gene. C21orf25 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf25, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf25 BINDING SITE, designated SEQ ID:31795, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16888] Another function of VGAM316 is therefore inhibition of Chromosome 21 Open Reading Frame 25 (C21orf25, Accession XM_032945). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf25. Cerebellin 1 Precursor (CBLN1, Accession NM_004352) is another VGAM316 host target gene. CBLN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CBLN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBLN1 BINDING SITE, designated SEQ ID:10556, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16889] Another function of VGAM316 is therefore inhibition of Cerebellin 1 Precursor (CBLN1, Accession NM_004352). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBLN1. Cellular Repressor of E1A-stimulated Genes (CREG, Accession NM_003851) is another VGAM316 host target gene. CREG BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by CREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CREG BINDING SITE, designated SEQ ID:9945, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16890] Another function of VGAM316 is therefore inhibition of Cellular Repressor of E1A-stimulated Genes (CREG, Accession NM_003851). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CREG. FLJ10724 (Accession NM_018194) is another VGAM316 host target gene. FLJ10724 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10724, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10724 BINDING SITE, designated SEQ ID:20051, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16891] Another function of VGAM316 is therefore inhibition of

FLJ10724 (Accession NM_018194). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10724. FLJ14011 (Accession NM_022103) is another VGAM316 host target gene. FLJ14011 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ14011, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14011 BINDING SITE, designated SEQ ID:22648, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16892] Another function of VGAM316 is therefore inhibition of FLJ14011 (Accession NM_022103). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14011. FLJ23510 (Accession NM_024720) is another VGAM316 host target gene. FLJ23510 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23510, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ23510 BINDING SITE, designated SEQ ID:24055, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16893] Another function of VGAM316 is therefore inhibition of FLJ23510 (Accession NM_024720). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23510. Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM_014271) is another VGAM316 host target gene. IL1RAPL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL1RAPL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL1RAPL1 BINDING SITE, designated SEQ ID:15550, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16894] Another function of VGAM316 is therefore inhibition of Interleukin 1 Receptor Accessory Protein-like 1 (IL1RAPL1, Accession NM_014271). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with IL1RAPL1.

KIAA0455 (Accession XM_051785) is another VGAM316 host target gene. KIAA0455 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0455, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0455 BINDING SITE, designated SEQ ID:35882, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16895] Another function of VGAM316 is therefore inhibition of KIAA0455 (Accession XM_051785). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0455. KIAA0945 (Accession NM_014952) is another VGAM316 host target gene. KIAA0945 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0945, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0945 BINDING SITE, designated SEQ ID:17289, to the

nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16896] Another function of VGAM316 is therefore inhibition of KIAA0945 (Accession NM_014952). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0945. NECL1 (Accession NM_021189) is another VGAM316 host target gene. NECL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NECL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NECL1 BINDING SITE, designated SEQ ID:22167, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16897] Another function of VGAM316 is therefore inhibition of NECL1 (Accession NM_021189). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NECL1. P311 (Accession NM_004772) is another VGAM316 host target gene. P311 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by P311, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P311 BINDING SITE, designated SEQ ID:11162, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16898] Another function of VGAM316 is therefore inhibition of P311 (Accession NM_004772). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P311. RAB10, Member RAS Oncogene Family (RAB10, Accession XM_097979) is another VGAM316 host target gene. RAB10 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB10, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB10 BINDING SITE, designated SEQ ID:41280, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16899] Another function of VGAM316 is therefore inhibition of RAB10, Member RAS Oncogene Family (RAB10, Accession

XM_097979). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB10. SR-BP1 (Accession NM_005866) is another VGAM316 host target gene. SR-BP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SR-BP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SR-BP1 BINDING SITE, designated SEQ ID:12486, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16900] Another function of VGAM316 is therefore inhibition of SR-BP1 (Accession NM_005866). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SR-BP1. Transducer of ERBB2, 2 (TOB2, Accession XM_170995) is another VGAM316 host target gene. TOB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TOB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of TOB2 BINDING SITE, designated SEQ ID:45759, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16901] Another function of VGAM316 is therefore inhibition of Transducer of ERBB2, 2 (TOB2, Accession XM_170995). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TOB2. Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM_016598) is another VGAM316 host target gene. ZDHHC3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZDHHC3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZDHHC3 BINDING SITE, designated SEQ ID:18687, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16902] Another function of VGAM316 is therefore inhibition of Zinc Finger, DHHC Domain Containing 3 (ZDHHC3, Accession NM_016598). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with ZDHHC3. LOC115265 (Accession XM_055596) is another VGAM316 host target gene. LOC115265 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC115265, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115265 BINDING SITE, designated SEQ ID:36308, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16903] Another function of VGAM316 is therefore inhibition of LOC115265 (Accession XM_055596). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115265. LOC145719 (Accession XM_096848) is another VGAM316 host target gene. LOC145719 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC145719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145719 BINDING SITE, designated SEQ ID:40569, to

the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16904] Another function of VGAM316 is therefore inhibition of LOC145719 (Accession XM_096848). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145719. LOC145720 (Accession XM_096846) is another VGAM316 host target gene. LOC145720 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145720, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145720 BINDING SITE, designated SEQ ID:40559, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16905] Another function of VGAM316 is therefore inhibition of LOC145720 (Accession XM_096846). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145720. LOC147671 (Accession XM_085844) is another VGAM316 host target gene. LOC147671 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC147671, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC147671 BINDING SITE, designated SEQ ID:38374, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16906] Another function of VGAM316 is therefore inhibition of LOC147671 (Accession XM_085844). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC147671. LOC148137 (Accession NM_144692) is another VGAM316 host target gene. LOC148137 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148137, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148137 BINDING SITE, designated SEQ ID:29518, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16907] Another function of VGAM316 is therefore inhibition of LOC148137 (Accession NM_144692). Accordingly, utilities

of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148137. LOC150295 (Accession XM_097868) is another VGAM316 host target gene. LOC150295 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC150295, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC150295 BINDING SITE, designated SEQ ID:41179, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16908] Another function of VGAM316 is therefore inhibition of LOC150295 (Accession XM_097868). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150295. LOC197117 (Accession XM_116989) is another VGAM316 host target gene. LOC197117 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC197117, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC197117 BINDING SITE, designated SEQ ID:43192, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16909] Another function of VGAM316 is therefore inhibition of LOC197117 (Accession XM_116989). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC197117. LOC221755 (Accession XM_166465) is another VGAM316 host target gene. LOC221755 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221755, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221755 BINDING SITE, designated SEQ ID:44385, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16910] Another function of VGAM316 is therefore inhibition of LOC221755 (Accession XM_166465). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221755. LOC254020 (Accession XM_171198) is another VGAM316 host target gene. LOC254020 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254020, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254020 BINDING SITE, designated SEQ ID:45987, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16911] Another function of VGAM316 is therefore inhibition of LOC254020 (Accession XM_171198). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254020. LOC91250 (Accession XM_037135) is another VGAM316 host target gene. LOC91250 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91250, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91250 BINDING SITE, designated SEQ ID:32547, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16912] Another function of VGAM316 is therefore inhibition of

LOC91250 (Accession XM_037135). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91250. LOC92539 (Accession XM_045632) is another VGAM316 host target gene. LOC92539 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92539 BINDING SITE, designated SEQ ID:34494, to the nucleotide sequence of VGAM316 RNA, herein designated VGAM RNA, also designated SEQ ID:3027.

[16913] Another function of VGAM316 is therefore inhibition of LOC92539 (Accession XM_045632). Accordingly, utilities of VGAM316 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92539. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 317 (VGAM317) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is

known in the art.

[16914] VGAM317 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM317 was detected is described hereinabove with reference to Figs. 1–8.

[16915] VGAM317 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 3. VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16916] VGAM317 gene encodes a VGAM317 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM317 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM317 precursor RNA is designated SEQ ID:303, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:303 is located at position 1398 relative to the genome of Cryphonectria Hypovirus 3.

[16917] VGAM317 precursor RNA folds onto itself, forming VGAM317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional

`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[16918] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM317 folded precursor RNA into VGAM317 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM317 RNA is designated SEQ ID:3028, and
is provided hereinbelow with reference to the sequence
listing part.

[16919] VGAM317 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM317 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM317 host target RNA comprises
three regions, as is typical of mRNA of a protein coding
gene: a 5` untranslated region, a protein coding region

and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16920] VGAM317 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM317 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM317 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR

and 5`UTR regions.

[16921] The complementary binding of VGAM317 RNA, herein designated VGAM RNA, to host target binding sites on VGAM317 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM317 host target RNA into VGAM317 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16922] It is appreciated that VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM317 host target genes. The mRNA of each one of this plurality of VGAM317 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM317 RNA, herein designated VGAM RNA, and which when bound by VGAM317 RNA causes inhibition of translation of respective one or more VGAM317 host target proteins.

[16923] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM317 gene, herein designated VGAM GENE, on one or

more VGAM317 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16924] It is yet further appreciated that a function of VGAM317 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 3. Specific functions, and accordingly utilities, of VGAM317 correlate with, and may be deduced from, the identity of the host target genes which VGAM317 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [16925] Nucleotide sequences of the VGAM317 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM317 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM317 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM317 are further described hereinbelow with reference to Table 1.
- [16926] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM317 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM317 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [16927] As mentioned hereinabove with reference to Fig. 1, a function of VGAM317 gene, herein designated VGAM is inhibition of expression of VGAM317 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM317 correlate with, and may be deduced from, the identity of the target genes which VGAM317 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.
- [16928] Suppressor of Cytokine Signaling 5 (SOCS5, Accession

NM_014011) is a VGAM317 host target gene. SOCS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOCS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOCS5 BINDING SITE, designated SEQ ID:15224, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16929] A function of VGAM317 is therefore inhibition of Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOCS5. DKFZp434F1719 (Accession NM_032248) is another VGAM317 host target gene. DKFZp434F1719 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZp434F1719, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp434F1719 BINDING SITE, designated SEQ ID:25989, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM

RNA, also designated SEQ ID:3028.

[16930] Another function of VGAM317 is therefore inhibition of DKFZp434F1719 (Accession NM_032248). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp434F1719. KIAA0841 (Accession XM_049237) is another VGAM317 host target gene. KIAA0841 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0841 BINDING SITE, designated SEQ ID:35358, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16931] Another function of VGAM317 is therefore inhibition of KIAA0841 (Accession XM_049237). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0841. KIAA1317 (Accession XM_098368) is another VGAM317 host target gene. KIAA1317 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1317, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1317 BINDING SITE, designated SEQ ID:41625, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16932] Another function of VGAM317 is therefore inhibition of KIAA1317 (Accession XM_098368). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1317. KIAA1546 (Accession XM_042301) is another VGAM317 host target gene. KIAA1546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1546 BINDING SITE, designated SEQ ID:33713, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16933] Another function of VGAM317 is therefore inhibition of KIAA1546 (Accession XM_042301). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA1546. Mesoderm Development Candidate 2 (MESDC2, Accession XM_051854) is another VGAM317 host target gene. MESDC2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MESDC2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MESDC2 BINDING SITE, designated SEQ ID:35889, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16934] Another function of VGAM317 is therefore inhibition of Mesoderm Development Candidate 2 (MESDC2, Accession XM_051854). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MESDC2. LOC163479 (Accession XM_088925) is another VGAM317 host target gene. LOC163479 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC163479, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nu-

cleotide sequences of LOC163479 BINDING SITE, designated SEQ ID:39956, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16935] Another function of VGAM317 is therefore inhibition of LOC163479 (Accession XM_088925). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC163479. LOC51696 (Accession NM_016217) is another VGAM317 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18309, to the nucleotide sequence of VGAM317 RNA, herein designated VGAM RNA, also designated SEQ ID:3028.

[16936] Another function of VGAM317 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM317 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 318 (VGAM318) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16937] VGAM318 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM318 was detected is described hereinabove with reference to Figs. 1–8.

[16938] VGAM318 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Cryphonectria Hypovirus 3. VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16939] VGAM318 gene encodes a VGAM318 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM318 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM318 precursor RNA is designated SEQ ID:304, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:304 is

located at position 739 relative to the genome of Cryphonectria Hypovirus 3.

[16940] VGAM318 precursor RNA folds onto itself, forming VGAM318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16941] An enzyme complex designated DICER COMPLEX, `dices` the VGAM318 folded precursor RNA into VGAM318 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM318 RNA is designated SEQ ID:3029, and is provided hereinbelow with reference to the sequence listing part.

[16942] VGAM318 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM318 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[16943] VGAM318 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM318 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM318 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM318 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[16944] The complementary binding of VGAM318 RNA, herein designated VGAM RNA, to host target binding sites on VGAM318 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM318 host target RNA into VGAM318 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16945] It is appreciated that VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM318 host target genes. The mRNA of each one of this plurality of VGAM318 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM318 RNA, herein designated VGAM RNA, and which when bound by VGAM318 RNA causes inhibition of translation of respective one or more VGAM318

host target proteins.

[16946] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM318 gene, herein designated VGAM GENE, on one or more VGAM318 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16947] It is yet further appreciated that a function of VGAM318 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of viral infection by Cryphonectria Hypovirus 3.

Specific functions, and accordingly utilities, of VGAM318 correlate with, and may be deduced from, the identity of the host target genes which VGAM318 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16948] Nucleotide sequences of the VGAM318 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM318 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM318 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM318 are further described hereinbelow with reference to Table 1.

[16949] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM318 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM318 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16950] As mentioned hereinabove with reference to Fig. 1, a function of VGAM318 gene, herein designated VGAM is inhibition of expression of VGAM318 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM318 correlate with, and may be deduced from, the identity of the target genes which VGAM318 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16951] Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982) is a VGAM318 host target gene. PIK3R3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIK3R3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIK3R3 BINDING SITE, designated SEQ ID:30607, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16952] A function of VGAM318 is therefore inhibition of Phosphoinositide-3-kinase, Regulatory Subunit, Polypeptide 3 (p55, gamma) (PIK3R3, Accession XM_027982). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIK3R3. FLJ11342 (Accession NM_018394) is another VGAM318 host target gene. FLJ11342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ11342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11342 BINDING SITE, designated SEQ ID:20432, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16953] Another function of VGAM318 is therefore inhibition of FLJ11342 (Accession NM_018394). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11342. KIAA0397 (Accession XM_029438) is another VGAM318 host target gene. KIAA0397 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0397, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0397 BINDING SITE, designated SEQ ID:30893, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16954] Another function of VGAM318 is therefore inhibition of KIAA0397 (Accession XM_029438). Accordingly, utilities

of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0397. LOC149146 (Accession XM_086441) is another VGAM318 host target gene. LOC149146 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149146 BINDING SITE, designated SEQ ID:38655, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16955] Another function of VGAM318 is therefore inhibition of LOC149146 (Accession XM_086441). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149146. LOC164684 (Accession XM_092926) is another VGAM318 host target gene. LOC164684 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC164684, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC164684 BINDING SITE, designated SEQ ID:40158, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16956] Another function of VGAM318 is therefore inhibition of LOC164684 (Accession XM_092926). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164684. LOC200563 (Accession XM_117251) is another VGAM318 host target gene. LOC200563 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200563 BINDING SITE, designated SEQ ID:43320, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16957] Another function of VGAM318 is therefore inhibition of LOC200563 (Accession XM_117251). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200563. LOC253832 (Accession XM_170739) is another VGAM318 host target gene. LOC253832 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC253832, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253832 BINDING SITE, designated SEQ ID:45498, to the nucleotide sequence of VGAM318 RNA, herein designated VGAM RNA, also designated SEQ ID:3029.

[16958] Another function of VGAM318 is therefore inhibition of LOC253832 (Accession XM_170739). Accordingly, utilities of VGAM318 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC253832. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 319 (VGAM319) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16959] VGAM319 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM319 was detected is described hereinabove with reference to Figs. 1-8.

[16960] VGAM319 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus.

VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16961] VGAM319 gene encodes a VGAM319 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM319 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM319 precursor RNA is designated SEQ ID:305, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:305 is located at position 46864 relative to the genome of Myxoma Virus.

[16962] VGAM319 precursor RNA folds onto itself, forming VGAM319 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[16963] An enzyme complex designated DICER COMPLEX, `dices` the VGAM319 folded precursor RNA into VGAM319 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM319 RNA is designated SEQ ID:3030, and is provided hereinbelow with reference to the sequence listing part.

[16964] VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM319 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16965] VGAM319 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM319 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM319 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM319 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[16966] The complementary binding of VGAM319 RNA, herein designated VGAM RNA, to host target binding sites on VGAM319 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM319 host target RNA into VGAM319 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16967] It is appreciated that VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM319 host target genes. The mRNA of each one of this plurality of VGAM319 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM319 RNA, herein designated VGAM RNA, and which when bound by VGAM319 RNA causes inhibition of translation of respective one or more VGAM319 host target proteins.

[16968] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM319 gene, herein designated VGAM GENE, on one or more VGAM319 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16969] It is yet further appreciated that a function of VGAM319 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM319 correlate with, and may be deduced from, the identity of the host target genes which VGAM319 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16970] Nucleotide sequences of the VGAM319 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM319 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM319 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM319 are further described hereinbelow with reference to Table 1.

[16971] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM319 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM319 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16972] As mentioned hereinabove with reference to Fig. 1, a function of VGAM319 gene, herein designated VGAM is inhibition of expression of VGAM319 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM319 correlate with, and may be deduced from, the identity of the target genes which VGAM319 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16973] Leptin (obesity homolog, mouse) (LEP, Accession NM_000230) is a VGAM319 host target gene. LEP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the

complementarity of the nucleotide sequences of LEP BINDING SITE, designated SEQ ID:5734, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16974] A function of VGAM319 is therefore inhibition of Leptin (obesity homolog, mouse) (LEP, Accession NM_000230). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEP. FLJ20051 (Accession NM_019087) is another VGAM319 host target gene. FLJ20051 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20051, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20051 BINDING SITE, designated SEQ ID:21161, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16975] Another function of VGAM319 is therefore inhibition of FLJ20051 (Accession NM_019087). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20051. Integrin, Beta 5 (ITGB5, Accession XM_003029) is another

VGAM319 host target gene. ITGB5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ITGB5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ITGB5 BINDING SITE, designated SEQ ID:29922, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16976] Another function of VGAM319 is therefore inhibition of Integrin, Beta 5 (ITGB5, Accession XM_003029). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ITGB5. KIAA1784 (Accession XM_036660) is another VGAM319 host target gene. KIAA1784 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1784, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1784 BINDING SITE, designated SEQ ID:32483, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16977] Another function of VGAM319 is therefore inhibition of KIAA1784 (Accession XM_036660). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1784. MAIL (Accession NM_031419) is another VGAM319 host target gene. MAIL BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MAIL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAIL BINDING SITE, designated SEQ ID:25404, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16978] Another function of VGAM319 is therefore inhibition of MAIL (Accession NM_031419). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAIL. SDS3 (Accession XM_045014) is another VGAM319 host target gene. SDS3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by SDS3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of SDS3 BINDING SITE, designated SEQ ID:34321, to the nucleotide sequence of VGAM319 RNA, herein designated VGAM RNA, also designated SEQ ID:3030.

[16979] Another function of VGAM319 is therefore inhibition of SDS3 (Accession XM_045014). Accordingly, utilities of VGAM319 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SDS3. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 320 (VGAM320) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16980] VGAM320 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM320 was detected is described hereinabove with reference to Figs. 1–8.

[16981] VGAM320 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the

human genome.

[16982] VGAM320 gene encodes a VGAM320 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM320 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM320 precursor RNA is designated SEQ ID:306, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:306 is located at position 46583 relative to the genome of Myxoma Virus.

[16983] VGAM320 precursor RNA folds onto itself, forming VGAM320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[16984] An enzyme complex designated DICER COMPLEX, `dices` the VGAM320 folded precursor RNA into VGAM320 RNA, herein designated VGAM RNA, a single stranded ~22 nt

long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM320 RNA is designated SEQ ID:3031, and is provided hereinbelow with reference to the sequence listing part.

[16985] VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM320 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[16986] VGAM320 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM320 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide se-

quence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM320 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[16987] The complementary binding of VGAM320 RNA, herein designated VGAM RNA, to host target binding sites on VGAM320 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM320 host target RNA into VGAM320 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[16988] It is appreciated that VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM320 host target genes. The mRNA of each one of this plurality of VGAM320 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM320 RNA, herein designated VGAM RNA, and which when bound by VGAM320 RNA causes inhibition of translation of respective one or more VGAM320 host target proteins.

[16989] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM320 gene, herein designated VGAM GENE, on one or more VGAM320 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, al-

though specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[16990] It is yet further appreciated that a function of VGAM320 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM320 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM320 correlate with, and may be deduced from, the identity of the host target genes which VGAM320 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[16991] Nucleotide sequences of the VGAM320 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM320 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM320 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM320 are further described hereinbelow with reference to Table 1.

[16992] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of

Fig. 1, found on VGAM320 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM320 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[16993] As mentioned hereinabove with reference to Fig. 1, a function of VGAM320 gene, herein designated VGAM is inhibition of expression of VGAM320 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM320 correlate with, and may be deduced from, the identity of the target genes which VGAM320 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[16994] GRB2-associated Binding Protein 2 (GAB2, Accession NM_012296) is a VGAM320 host target gene. GAB2 BINDING SITE1 and GAB2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GAB2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GAB2 BINDING SITE1 and GAB2 BINDING SITE2, designated SEQ ID:14646 and SEQ ID:27842 respectively, to the nucleotide sequence of

VGAM320 RNA, herein designated VGAM RNA, also designated SEQ ID:3031.

[16995] A function of VGAM320 is therefore inhibition of GRB2-associated Binding Protein 2 (GAB2, Accession NM_012296), a gene which act as adapters for transmitting various signals. Accordingly, utilities of VGAM320 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GAB2. The function of GAB2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM53.FLJ13612 (Accession NM_025202) is another VGAM320 host target gene. FLJ13612 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13612, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13612 BINDING SITE, designated SEQ ID:24863, to the nucleotide sequence of VGAM320 RNA, herein designated VGAM RNA, also designated SEQ ID:3031.

[16996] Another function of VGAM320 is therefore inhibition of FLJ13612 (Accession NM_025202). Accordingly, utilities of

VGAM320 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13612. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 321 (VGAM321) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[16997] VGAM321 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM321 was detected is described hereinabove with reference to Figs. 1–8.

[16998] VGAM321 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus.

VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[16999] VGAM321 gene encodes a VGAM321 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM321 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM321 precursor RNA is designated SEQ

ID:307, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:307 is located at position 52219 relative to the genome of Myxoma Virus.

[17000] VGAM321 precursor RNA folds onto itself, forming VGAM321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17001] An enzyme complex designated DICER COMPLEX, `dices` the VGAM321 folded precursor RNA into VGAM321 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 87%) nucleotide sequence of VGAM321 RNA is designated SEQ ID:3032, and is provided hereinbelow with reference to the sequence

listing part.

[17002] VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM321 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17003] VGAM321 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM321 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM321 RNA, herein designated VGAM RNA, may

have a different number of host target binding sites in untranslated regions of a VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17004] The complementary binding of VGAM321 RNA, herein designated VGAM RNA, to host target binding sites on VGAM321 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM321 host target RNA into VGAM321 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17005] It is appreciated that VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM321 host target genes. The mRNA of each one of this plurality of VGAM321 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM321 RNA, herein designated VGAM

RNA, and which when bound by VGAM321 RNA causes inhibition of translation of respective one or more VGAM321 host target proteins.

[17006] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM321 gene, herein designated VGAM GENE, on one or more VGAM321 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17007] It is yet further appreciated that a function of VGAM321 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly,

utilities of VGAM321 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM321 correlate with, and may be deduced from, the identity of the host target genes which VGAM321 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

- [17008] Nucleotide sequences of the VGAM321 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM321 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM321 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM321 are further described hereinbelow with reference to Table 1.
- [17009] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM321 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM321 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [17010] As mentioned hereinabove with reference to Fig. 1, a function of VGAM321 gene, herein designated VGAM is

inhibition of expression of VGAM321 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM321 correlate with, and may be deduced from, the identity of the target genes which VGAM321 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17011] Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434) is a VGAM321 host target gene. DAAM2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DAAM2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DAAM2 BINDING SITE, designated SEQ ID:44328, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17012] A function of VGAM321 is therefore inhibition of Dishevelled Associated Activator of Morphogenesis 2 (DAAM2, Accession XM_166434), a gene which controls cell polarity and movement during development. Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

DAAM2. The function of DAAM2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM247. Estrogen-related Receptor Beta Like 1 (ESRRBL1, Accession NM_018010) is another VGAM321 host target gene. ESRRBL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ESRRBL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ESRRBL1 BINDING SITE, designated SEQ ID:19742, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17013] Another function of VGAM321 is therefore inhibition of Estrogen-related Receptor Beta Like 1 (ESRRBL1, Accession NM_018010). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ESRRBL1. Baculoviral IAP Repeat-containing 2 (BIRC2, Accession XM_040717) is another VGAM321 host target gene. BIRC2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by BIRC2, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BIRC2 BINDING SITE, designated SEQ ID:33371, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17014] Another function of VGAM321 is therefore inhibition of Baculoviral IAP Repeat-containing 2 (BIRC2, Accession XM_040717). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BIRC2. Chromobox Homolog 3 (HP1 gamma homolog, Drosophila) (CBX3, Accession NM_007276) is another VGAM321 host target gene. CBX3 BINDING SITE1 and CBX3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CBX3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CBX3 BINDING SITE1 and CBX3 BINDING SITE2, designated SEQ ID:14140 and SEQ ID:18660 respectively, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17015] Another function of VGAM321 is therefore inhibition of Chromobox Homolog 3 (HP1 gamma homolog, Drosophila) (CBX3, Accession NM_007276). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CBX3. KIAA1715 (Accession XM_042834) is another VGAM321 host target gene. KIAA1715 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1715, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1715 BINDING SITE, designated SEQ ID:33789, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17016] Another function of VGAM321 is therefore inhibition of KIAA1715 (Accession XM_042834). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1715. MFN1 (Accession NM_017927) is another VGAM321 host target gene. MFN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MFN1, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MFN1 BINDING SITE, designated SEQ ID:19602, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17017] Another function of VGAM321 is therefore inhibition of MFN1 (Accession NM_017927). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MFN1. Rab11-FIP2 (Accession NM_014904) is another VGAM321 host target gene. Rab11-FIP2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by Rab11-FIP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of Rab11-FIP2 BINDING SITE, designated SEQ ID:17095, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17018] Another function of VGAM321 is therefore inhibition of Rab11-FIP2 (Accession NM_014904). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with Rab11-FIP2. SNRK (Accession NM_017719) is another VGAM321 host target gene. SNRK BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SNRK, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SNRK BINDING SITE, designated SEQ ID:19310, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17019] Another function of VGAM321 is therefore inhibition of SNRK (Accession NM_017719). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SNRK. LOC155434 (Accession XM_098723) is another VGAM321 host target gene. LOC155434 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC155434, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC155434 BINDING SITE, designated SEQ ID:41770, to the nucleotide se-

quence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17020] Another function of VGAM321 is therefore inhibition of LOC155434 (Accession XM_098723). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC155434. LOC158563 (Accession XM_088606) is another VGAM321 host target gene. LOC158563 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158563, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158563 BINDING SITE, designated SEQ ID:39867, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17021] Another function of VGAM321 is therefore inhibition of LOC158563 (Accession XM_088606). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158563. LOC257358 (Accession XM_173138) is another VGAM321 host target gene. LOC257358 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC257358, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257358 BINDING SITE, designated SEQ ID:46387, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17022] Another function of VGAM321 is therefore inhibition of LOC257358 (Accession XM_173138). Accordingly, utilities of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257358. LOC91660 (Accession XM_039902) is another VGAM321 host target gene. LOC91660 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91660, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91660 BINDING SITE, designated SEQ ID:33206, to the nucleotide sequence of VGAM321 RNA, herein designated VGAM RNA, also designated SEQ ID:3032.

[17023] Another function of VGAM321 is therefore inhibition of LOC91660 (Accession XM_039902). Accordingly, utilities

of VGAM321 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91660. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 322 (VGAM322) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17024] VGAM322 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM322 was detected is described hereinabove with reference to Figs. 1–8.

[17025] VGAM322 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17026] VGAM322 gene encodes a VGAM322 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM322 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide se–

quence of VGAM322 precursor RNA is designated SEQ ID:308, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:308 is located at position 88846 relative to the genome of Myxoma Virus.

[17027] VGAM322 precursor RNA folds onto itself, forming VGAM322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17028] An enzyme complex designated DICER COMPLEX, `dices` the VGAM322 folded precursor RNA into VGAM322 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 76%) nucleotide sequence of VGAM322 RNA is designated SEQ ID:3033, and

is provided hereinbelow with reference to the sequence listing part.

[17029] VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM322 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17030] VGAM322 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM322 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limit-

ing – VGAM322 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17031] The complementary binding of VGAM322 RNA, herein designated VGAM RNA, to host target binding sites on VGAM322 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM322 host target RNA into VGAM322 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17032] It is appreciated that VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM322 host target genes. The mRNA of each one of this plurality of VGAM322 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly com-

plementary to VGAM322 RNA, herein designated VGAM RNA, and which when bound by VGAM322 RNA causes inhibition of translation of respective one or more VGAM322 host target proteins.

[17033] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM322 gene, herein designated VGAM GENE, on one or more VGAM322 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17034] It is yet further appreciated that a function of VGAM322 is inhibition of expression of host target genes, as part of a

novel viral mechanism of attacking a host. Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM322 correlate with, and may be deduced from, the identity of the host target genes which VGAM322 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17035] Nucleotide sequences of the VGAM322 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM322 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM322 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM322 are further described hereinbelow with reference to Table 1.

[17036] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM322 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM322 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17037] As mentioned hereinabove with reference to Fig. 1, a

function of VGAM322 gene, herein designated VGAM is inhibition of expression of VGAM322 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM322 correlate with, and may be deduced from, the identity of the target genes which VGAM322 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17038] LY95 (Accession NM_004828) is a VGAM322 host target gene. LY95 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LY95, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LY95 BINDING SITE, designated SEQ ID:11241, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17039] A function of VGAM322 is therefore inhibition of LY95 (Accession NM_004828). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LY95. Reelin (RELN, Accession XM_168628) is another VGAM322 host target gene. RELN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by RELN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RELN BINDING SITE, designated SEQ ID:45283, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17040] Another function of VGAM322 is therefore inhibition of Reelin (RELN, Accession XM_168628), a gene which regulates microtubule function in neurons and neuronal migration. Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RELN. The function of RELN and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM35. LHX6 (Accession NM_014368) is another VGAM322 host target gene. LHX6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LHX6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LHX6 BINDING SITE, designated SEQ ID:15699,

to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17041] Another function of VGAM322 is therefore inhibition of LHX6 (Accession NM_014368). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LHX6. RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733) is another VGAM322 host target gene. RAB40A BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by RAB40A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB40A BINDING SITE, designated SEQ ID:39925, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17042] Another function of VGAM322 is therefore inhibition of RAB40A, Member RAS Oncogene Family (RAB40A, Accession XM_088733). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB40A. LOC116113 (Accession XM_166413) is another VGAM322 host target

gene. LOC116113 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116113, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116113 BINDING SITE, designated SEQ ID:44288, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17043] Another function of VGAM322 is therefore inhibition of LOC116113 (Accession XM_166413). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116113. LOC200107 (Accession XM_114121) is another VGAM322 host target gene. LOC200107 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200107, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200107 BINDING SITE, designated SEQ ID:42708, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17044] Another function of VGAM322 is therefore inhibition of LOC200107 (Accession XM_114121). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200107. LOC206426 (Accession XM_116505) is another VGAM322 host target gene. LOC206426 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC206426, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC206426 BINDING SITE, designated SEQ ID:43114, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17045] Another function of VGAM322 is therefore inhibition of LOC206426 (Accession XM_116505). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC206426. LOC257017 (Accession XM_173227) is another VGAM322 host target gene. LOC257017 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC257017, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC257017 BINDING SITE, designated SEQ ID:46497, to the nucleotide sequence of VGAM322 RNA, herein designated VGAM RNA, also designated SEQ ID:3033.

[17046] Another function of VGAM322 is therefore inhibition of LOC257017 (Accession XM_173227). Accordingly, utilities of VGAM322 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC257017. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 323 (VGAM323) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17047] VGAM323 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM323 was detected is described hereinabove with reference to Figs. 1–8.

[17048] VGAM323 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Myxoma Virus. VGAM323 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[17049] VGAM323 gene encodes a VGAM323 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM323 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM323 precursor RNA is designated SEQ ID:309, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:309 is located at position 145414 relative to the genome of Myxoma Virus.

[17050] VGAM323 precursor RNA folds onto itself, forming VGAM323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17051] An enzyme complex designated DICER COMPLEX, `dices` the VGAM323 folded precursor RNA into VGAM323 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 75%) nucleotide sequence of VGAM323 RNA is designated SEQ ID:3034, and is provided hereinbelow with reference to the sequence listing part.

[17052] VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM323 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17053] VGAM323 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM323 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM323 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17054] The complementary binding of VGAM323 RNA, herein designated VGAM RNA, to host target binding sites on VGAM323 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM323 host target RNA into VGAM323 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[17055] It is appreciated that VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM323 host target genes. The mRNA of each one of this plurality of VGAM323 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM323 RNA, herein designated VGAM RNA, and which when bound by VGAM323 RNA causes inhibition of translation of respective one or more VGAM323 host target proteins.

[17056] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM323 gene, herein designated VGAM GENE, on one or more VGAM323 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17057] It is yet further appreciated that a function of VGAM323 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of viral infection by Myxoma Virus. Specific functions, and accordingly utilities, of VGAM323 correlate with, and may be deduced from, the identity of the host target genes which VGAM323 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17058] Nucleotide sequences of the VGAM323 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM323 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM323 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM323 are further described hereinbelow with reference to Table 1.

[17059] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM323 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM323 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17060] As mentioned hereinabove with reference to Fig. 1, a function of VGAM323 gene, herein designated VGAM is inhibition of expression of VGAM323 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM323 correlate with, and may be deduced from, the identity of the target genes which VGAM323 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17061] Adenosine Deaminase, RNA-specific (ADAR, Accession NM_001111) is a VGAM323 host target gene. ADAR BINDING SITE1 through ADAR BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ADAR, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADAR BINDING SITE1 through ADAR BINDING SITE3, designated SEQ ID:6776, SEQ ID:17962

and SEQ ID:17969 respectively, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17062] A function of VGAM323 is therefore inhibition of Adenosine Deaminase, RNA-specific (ADAR, Accession NM_001111), a gene which converts adenosine to inosine in double-stranded RNA. Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADAR. The function of ADAR has been established by previous studies. Double-stranded RNA-specific adenosine deaminase (DSRAD) was identified as a developmentally regulated dsRNA unwinding activity in early antisense experiments with *Xenopus* oocytes (Bass and Weintraub, 1988). The enzyme converts adenosine to inosine in dsRNA, which destabilizes the dsRNA helix. The RNA modifying activity of DSRAD is important for various functions. Among these are site-specific RNA editing of transcripts of the glutamate receptors (see OMIM Ref. No. 138248), which are channels for the neurotransmitter L-glutamate in the brain. DSRAD also functions to modify viral RNA genomes and may be responsible for hypermutation of certain negative-stranded viruses, such as measles, which

may result in lethal measles inclusion body encephalitis (Weier et al., 1995). By fluorescence in situ hybridization, Weier et al. (1995) mapped the DSRAD gene to 1q21.1–q21.2, centromeric to the marker D1S1705. Wang et al. (1995) mapped the DRADA gene to 1q21 by fluorescence in situ hybridization. By FISH, Weier et al. (2000) mapped the mouse homolog (Adar) to chromosome 3F2. Animal model experiments lend further support to the function of ADAR. Wang et al. (2000) knocked out the Adar1 gene in mice by targeted disruption and found that heterozygosity for the Adar1 knockout causes embryonic lethality.

[17063] It is appreciated that the abovementioned animal model for ADAR is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17064] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17065] Weier, H.–U. G.; George, C. X.; Greulich, K. M.; Samuel, C. E. : The interferon–inducible, double–stranded RNA–specific adenosine deaminase gene (DSRAD) maps to human chromosome 1q21.1–21.2. Genomics 30: 372–375,

1995. ; and

[17066] Wang, Q.; Khillan, J.; Gadue, P.; Nishikura, K. : Requirement of the RNA editing deaminase ADAR1 gene for embryonic erythropoiesis. Science 290: 1765–1768, 2000.

[17067] Further studies establishing the function and utilities of ADAR are found in John Hopkins OMIM database record ID 601059, and in cited publications numbered 7151–7158 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM_000620) is another VGAM323 host target gene. NOS1 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NOS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NOS1 BINDING SITE, designated SEQ ID:6229, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17068] Another function of VGAM323 is therefore inhibition of Nitric Oxide Synthase 1 (neuronal) (NOS1, Accession NM_000620), a gene which produces nitric oxide (no) which is a messenger molecule with diverse functions

throughout the body. Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NOS1. The function of NOS1 has been established by previous studies. Bredt et al. (1991) cloned a cDNA for the neuronal form of nitric oxide (NO) synthase and studied its expression. The only mammalian protein with close sequence similarity was cytochrome P450 reductase. Magee et al. (1996) used PCR to clone a novel form of neuronal NOS from rat penile RNA. This NOS cDNA was termed PnNOS for 'penile neuronal NOS.' Sequencing revealed that the PnNOS cDNA was identical to rat cerebellar neuronal NOS1 except for a 102-bp insertion in PnNOS, indicating that PnNOS is a novel isoform. PCR of a human penile cDNA library confirmed that this insert is present in human DNA at the same location. Repetition of RT-PCR showed PnNOS to be the only form of NOS1 expressed in rat penis, urethra, prostate, and skeletal muscle. The PnNOS form was also present in rat cerebellum, liver, and pelvic plexus, although less abundantly than the shorter isoform. The authors postulated that PnNOS may be responsible for the synthesis of nitric oxide during penile erection and may be involved in control of the tone of the urethra, prostate,

and bladder. Animal model experiments lend further support to the function of NOS1. Mice with targeted disruption of neuronal NO synthase display grossly normal appearance, locomotor activity, breeding, long-term potentiation, and long-term depression. NOS1-deficient mice are resistant to neural stroke damage following middle cerebral artery ligation. Nelson et al. (1995) reported a large increase in aggressive behavior and excessive, inappropriate sexual behavior in NOS1 'knockout' mice. Initial observations indicated that male NOS1-deficient mice engaged in chronic aggressive behavior, not apparent among NOS1-deficient female mice or wildtype male or female mice housed together. Relevance of the observations to human behavior was suggested.

[17069] It is appreciated that the abovementioned animal model for NOS1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17070] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17071] Magee, T.; Fuentes, A. M.; Garban, H.; Rajavashisth, T.; Marquez, D.; Rodriguez, J. A.; Rajfer, J.; Gonzalez-Ca-

david, N. F. : Cloning of a novel neuronal nitric oxide synthase expressed in penis and lower urinary tract. Biochem. Biophys. Res. Commun. 226: 145–151, 1996. ; and

[17072] Nelson, R. J.; Demas, G. E.; Huang, P. L.; Fishman, M. C.; Dawson, V. L.; Dawson, T. M.; Snyder, S. H. : Behavioural abnormalities in male mice lacking neuronal nitric oxide synthase. N.

[17073] Further studies establishing the function and utilities of NOS1 are found in John Hopkins OMIM database record ID 163731, and in cited publications numbered 11031–1864, 1854, 1865, 327 and 2729–2731 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 3 (formerly 2B), Regulatory Subunit B, 19kDa, Alpha Isoform (calcineurin B, type I) (PPP3R1, Accession XM_084103) is another VGAM323 host target gene. PPP3R1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP3R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP3R1 BINDING SITE, designated SEQ ID:37531, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA,

also designated SEQ ID:3034.

[17074] Another function of VGAM323 is therefore inhibition of Protein Phosphatase 3 (formerly 2B), Regulatory Subunit B, 19kDa, Alpha Isoform (calcineurin B, type I) (PPP3R1, Accession XM_084103), a gene which is a regulatory subunit of calcineurin, a calcium-dependent, calmodulin stimulated protein phosphatase 3. Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PPP3R1. The function of PPP3R1 has been established by previous studies. Calcineurin, a calmodulin-regulated protein phosphatase, is found in the cells of all eukaryotes ranging from yeast to mammals. Wang et al. (1996) described this heterodimeric protein as having a 19-kD $\text{Ca}(2+)$ -binding regulatory subunit, calcineurin B, and a 58- to 59-kD catalytic subunit, calcineurin A. One gene encodes calcineurin B in all tissues except testis, and it is highly conserved at the level of both protein and DNA sequences in eukaryotes. In contrast, there are 2 major isoforms, alpha (OMIM Ref. No. 114105) and beta (OMIM Ref. No. 114106), of calcineurin A encoded by separate genes located on different human chromosomes. A third isoform, A-gamma (OMIM Ref. No. 114107), is unique to

testis. Additional diversity of calcineurin A is created by alternative splicing of mRNAs. Calcineurin is especially abundant in brain where it constitutes 1% of total protein. Animal model experiments lend further support to the function of PPP3R1. Using conditional gene-targeting techniques, Zeng et al. (2001) created mice in which Cnb1 activity was disrupted specifically in the adult forebrain. At hippocampal Schaffer collateral-CA1 synapses, long-term depression (LTD) was significantly diminished, and there was a significant shift in the LTD/long-term potentiation (LTP) modification threshold in mutant mice. Although performance was normal in hippocampus-dependent reference memory tasks, including contextual fear conditioning and the Morris water maze, the mutant mice were impaired in hippocampus-dependent working and episodic-like memory tasks, including the delayed matching-to-place task and the radial maze task. These results defined a critical role for calcineurin in bidirectional synaptic plasticity and suggested a novel mechanistic distinction between working/episodic-like memory and reference memory.

[17075] It is appreciated that the abovementioned animal model for PPP3R1 is acknowledged by those skilled in the art as

a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[17076] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17077] Zeng, H.; Chattarji, S.; Barbarosie, M.; Rondi-Reig, L.; Philpot, B. D.; Miyakawa, T.; Bear, M. F.; Tonegawa, S. : Forebrain-specific calcineurin knockout selectively impairs bidirectional synaptic plasticity and working/episodic-like memory. Cell 107: 617–629, 2001. ; and

[17078] Wang, M. G.; Yi, H.; Guerini, D.; Klee, C. B.; McBride, O. W. : Calcineurin A alpha (PPP3CA), calcineurin A beta (PPP3CB) and calcineurin B (PPP3R1) are located on human chromosomes 4.

[17079] Further studies establishing the function and utilities of PPP3R1 are found in John Hopkins OMIM database record ID 601302, and in sited publications numbered 6507–6509 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Splicing Factor, Arginine/serine-rich 1 (splicing factor 2, alternate splicing factor) (SFRS1, Accession NM_006924) is another VGAM323 host target gene. SFRS1 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region

of mRNA encoded by SFRS1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRS1 BINDING SITE, designated SEQ ID:13800, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17080] Another function of VGAM323 is therefore inhibition of Splicing Factor, Arginine/serine-rich 1 (splicing factor 2, alternate splicing factor) (SFRS1, Accession NM_006924), a gene which plays an essential role in pre-mRNA splicing. Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRS1. The function of SFRS1 has been established by previous studies. Alternative mRNA splicing plays an important role in development and differentiation; many transcripts are spliced differently in distinct cell types and tissues. Bermingham et al. (1995) stated that while examples of alternatively spliced transcripts are found, relatively little is known about the mechanisms involved in regulating the use of alternative splice sites. Both constitutive and alternative splicing occurs on spliceosomes, which are complex particles composed of

small nuclear ribonucleoproteins (OMIM Ref. No. snRNPs) and non-snRNP proteins. The SR family of non-snRNP splicing factors is characterized by the presence of an RNA recognition motif and a serine- and arginine-rich (SR) domain. SR proteins are required at early stages of spliceosome assembly, have distinct but overlapping specificities for different pre-mRNAs, and can alter splice site choice. These observations suggested SR proteins may be involved in the regulation of alternative splicing in vivo. Two of the SR proteins have been extensively characterized: ASF/SF2 (for 'alternative splicing factor/splicing factor-2') and SC35 (for 'splicing component, 35-kD'). The genes encoding these 2 factors are designated SFRS1 and SFRS2 (OMIM Ref. No. 600813), respectively. Krainer et al. (1991) had previously isolated a human cDNA for the pre-mRNA splicing factor referred to as SF2p33, which was later designated SFRS1. Other SR proteins include SFRS4 (OMIM Ref. No. 601940), SFRS5 (OMIM Ref. No. 600914), SFRS6 (OMIM Ref. No. 601944), and SFRS8 (OMIM Ref. No. 601945). Pollard et al. (2000) sought to determine if the nuclear concentrations of the trans-acting splicing regulators SF2/ASF and HNRNPA1 (OMIM Ref. No. 164017) and its splice variant, HNRNPA1B, are fundamental in regulat-

ing the expression of specific protein isoforms derived from alternative splicing of single pre-mRNA transcripts. SF2/ASF and HNRNPA1/A1B expression was determined in paired upper (OMIM Ref. No. corpus) and lower segment myometrial samples taken from individual women at term or during spontaneous labor and compared with nonpregnant control samples using specific monoclonal antibodies. SF2/ASF levels were substantially increased in the lower uterine region, and this was associated with a parallel decrease in levels of HNRNPA1/A1B during gestation. Conversely, the opposite pattern was observed within the upper uterine region during pregnancy, where HNRNPA1/A1B was significantly upregulated and SF2/ASF levels were much lower than those found in the lower uterine segment. The authors concluded that differential expression of HNRNPA1/A1B and SF2/ASF in the upper and lower uterine segments may have a primary role in defining the formation of specific myometrial protein species associated with the known contractile and relaxatory properties of these regions before and during parturition.

[17081] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [17082] Bermingham, J. R., Jr.; Arden, K. C.; Naumova, A. K.; Sapienza, C.; Viars, C. S.; Fu, X.-D.; Khotz, J.; Manley, J. L.; Rosenfeld, M. G. : Chromosomal localization of mouse and human genes encoding the splicing factors ASF/SF2 (SFRS1) and SC-35 (SFRS2). *Genomics* 29: 70-79, 1995. ; and
- [17083] Pollard, A. J.; Sparey, C.; Robson, S. C.; Krainer, A. R.; Europe-Finner, G. N. : Spatio-temporal expression of the trans-acting splicing factors SF2/ASF and heterogeneous ribonuclear prote.
- [17084] Further studies establishing the function and utilities of SFRS1 are found in John Hopkins OMIM database record ID 600812, and in cited publications numbered 7138, 172 and 7139 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274) is another VGAM323 host target gene. AKAP6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AKAP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

AKAP6 BINDING SITE, designated SEQ ID:10491, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17085] Another function of VGAM323 is therefore inhibition of A Kinase (PRKA) Anchor Protein 6 (AKAP6, Accession NM_004274). Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AKAP6. KIAA1843 (Accession XM_030838) is another VGAM323 host target gene. KIAA1843 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1843, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1843 BINDING SITE, designated SEQ ID:31163, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17086] Another function of VGAM323 is therefore inhibition of KIAA1843 (Accession XM_030838). Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1843. P37NB (Accession NM_005824) is another

VGAM323 host target gene. P37NB BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by P37NB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of P37NB BINDING SITE, designated SEQ ID:12437, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17087] Another function of VGAM323 is therefore inhibition of P37NB (Accession NM_005824). Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with P37NB. Solute Carrier Family 37 (glycerol-3-phosphate transporter), Member 1 (SLC37A1, Accession NM_018964) is another VGAM323 host target gene. SLC37A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC37A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC37A1 BINDING SITE, designated SEQ ID:21036, to the nucleotide sequence of VGAM323 RNA, herein designated

VGAM RNA, also designated SEQ ID:3034.

[17088] Another function of VGAM323 is therefore inhibition of Solute Carrier Family 37 (glycerol-3-phosphate transporter), Member 1 (SLC37A1, Accession NM_018964). Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC37A1. LOC256502 (Accession XM_170546) is another VGAM323 host target gene. LOC256502 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC256502, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC256502 BINDING SITE, designated SEQ ID:45366, to the nucleotide sequence of VGAM323 RNA, herein designated VGAM RNA, also designated SEQ ID:3034.

[17089] Another function of VGAM323 is therefore inhibition of LOC256502 (Accession XM_170546). Accordingly, utilities of VGAM323 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC256502. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the

present invention, referred to here as Viral Genomic Address Messenger 324 (VGAM324) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17090] VGAM324 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM324 was detected is described hereinabove with reference to Figs. 1–8.

[17091] VGAM324 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17092] VGAM324 gene encodes a VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM324 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM324 precursor RNA is designated SEQ ID:310, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:310 is located at position 65828 relative to the genome of Rabbit

Fibroma Virus.

[17093] VGAM324 precursor RNA folds onto itself, forming VGAM324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17094] An enzyme complex designated DICER COMPLEX, `dices` the VGAM324 folded precursor RNA into VGAM324 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 84%) nucleotide sequence of VGAM324 RNA is designated SEQ ID:3035, and is provided hereinbelow with reference to the sequence listing part.

[17095] VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger

RNA, VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM324 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17096] VGAM324 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM324 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM324 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA. It is further

appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17097] The complementary binding of VGAM324 RNA, herein designated VGAM RNA, to host target binding sites on VGAM324 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM324 host target RNA into VGAM324 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17098] It is appreciated that VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM324 host target genes. The mRNA of each one of this plurality of VGAM324 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM324 RNA, herein designated VGAM RNA, and which when bound by VGAM324 RNA causes inhibition of translation of respective one or more VGAM324 host target proteins.

[17099] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM324 gene, herein designated VGAM GENE, on one or more VGAM324 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17100] It is yet further appreciated that a function of VGAM324 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM324 cor-

relate with, and may be deduced from, the identity of the host target genes which VGAM324 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17101] Nucleotide sequences of the VGAM324 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM324 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM324 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM324 are further described hereinbelow with reference to Table 1.

[17102] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM324 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM324 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17103] As mentioned hereinabove with reference to Fig. 1, a function of VGAM324 gene, herein designated VGAM is inhibition of expression of VGAM324 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM324 correlate with, and may be deduced

from, the identity of the target genes which VGAM324 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17104] Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession NM_000091) is a VGAM324 host target gene. COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by COL4A3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of COL4A3 BINDING SITE1 through COL4A3 BINDING SITE3, designated SEQ ID:5545, SEQ ID:25352 and SEQ ID:25358 respectively, to the nucleotide sequence of VGAM324 RNA, herein designated VGAM RNA, also designated SEQ ID:3035.

[17105] A function of VGAM324 is therefore inhibition of Collagen, Type IV, Alpha 3 (Goodpasture antigen) (COL4A3, Accession NM_000091). Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with COL4A3. Period Homolog 3 (Drosophila) (PER3, Accession NM_016831) is another VGAM324 host target gene. PER3 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PER3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PER3 BINDING SITE, designated SEQ ID:18820, to the nucleotide sequence of VGAM324 RNA, herein designated VGAM RNA, also designated SEQ ID:3035.

[17106] Another function of VGAM324 is therefore inhibition of Period Homolog 3 (Drosophila) (PER3, Accession NM_016831). Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PER3. Yes-associated Protein 1, 65kDa (YAP1, Accession NM_006106) is another VGAM324 host target gene. YAP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by YAP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of YAP1 BINDING SITE, designated SEQ ID:12752, to the nucleotide sequence of VGAM324 RNA, herein designated VGAM RNA, also designated SEQ ID:3035.

[17107] Another function of VGAM324 is therefore inhibition of Yes-associated Protein 1, 65kDa (YAP1, Accession NM_006106). Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with YAP1. LOC201627 (Accession XM_114353) is another VGAM324 host target gene. LOC201627 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC201627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC201627 BINDING SITE, designated SEQ ID:42894, to the nucleotide sequence of VGAM324 RNA, herein designated VGAM RNA, also designated SEQ ID:3035.

[17108] Another function of VGAM324 is therefore inhibition of LOC201627 (Accession XM_114353). Accordingly, utilities of VGAM324 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC201627. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 325 (VGAM325) viral gene, which modu-

lates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17109] VGAM325 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM325 was detected is described hereinabove with reference to Figs. 1–8.

[17110] VGAM325 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17111] VGAM325 gene encodes a VGAM325 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM325 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM325 precursor RNA is designated SEQ ID:311, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:311 is located at position 66316 relative to the genome of Rabbit Fibroma Virus.

[17112] VGAM325 precursor RNA folds onto itself, forming

VGAM325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17113] An enzyme complex designated DICER COMPLEX, `dices` the VGAM325 folded precursor RNA into VGAM325 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 73%) nucleotide sequence of VGAM325 RNA is designated SEQ ID:3036, and is provided hereinbelow with reference to the sequence listing part.

[17114] VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM325 host target RNA comprises

three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17115] VGAM325 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM325 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM325 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example

only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17116] The complementary binding of VGAM325 RNA, herein designated VGAM RNA, to host target binding sites on VGAM325 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM325 host target RNA into VGAM325 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17117] It is appreciated that VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM325 host target genes. The mRNA of each one of this plurality of VGAM325 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM325 RNA, herein designated VGAM RNA, and which when bound by VGAM325 RNA causes inhibition of translation of respective one or more VGAM325 host target proteins.

[17118] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with

specific reference to translational inhibition exerted by VGAM325 gene, herein designated VGAM GENE, on one or more VGAM325 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17119] It is yet further appreciated that a function of VGAM325 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM325 correlate with, and may be deduced from, the identity of the host target genes which VGAM325 binds and inhibits, and

the function of these host target genes, as elaborated hereinbelow.

[17120] Nucleotide sequences of the VGAM325 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM325 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM325 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM325 are further described hereinbelow with reference to Table 1.

[17121] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM325 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM325 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17122] As mentioned hereinabove with reference to Fig. 1, a function of VGAM325 gene, herein designated VGAM is inhibition of expression of VGAM325 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM325 correlate with, and may be deduced from, the identity of the target genes which VGAM325 binds and inhibits, and the function of these target genes,

as elaborated hereinbelow.

[17123] ABLIM (Accession NM_002313) is a VGAM325 host target gene. ABLIM BINDING SITE1 and ABLIM BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by ABLIM, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABLIM BINDING SITE1 and ABLIM BINDING SITE2, designated SEQ ID:8122 and SEQ ID:13555 respectively, to the nucleotide sequence of VGAM325 RNA, herein designated VGAM RNA, also designated SEQ ID:3036.

[17124] A function of VGAM325 is therefore inhibition of ABLIM (Accession NM_002313). Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABLIM. MGC13007 (Accession NM_032320) is another VGAM325 host target gene. MGC13007 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC13007, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC13007 BINDING

SITE, designated SEQ ID:26123, to the nucleotide sequence of VGAM325 RNA, herein designated VGAM RNA, also designated SEQ ID:3036.

[17125] Another function of VGAM325 is therefore inhibition of MGC13007 (Accession NM_032320). Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC13007. Ubiquitin Specific Protease 20 (USP20, Accession NM_006676) is another VGAM325 host target gene. USP20 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by USP20, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of USP20 BINDING SITE, designated SEQ ID:13504, to the nucleotide sequence of VGAM325 RNA, herein designated VGAM RNA, also designated SEQ ID:3036.

[17126] Another function of VGAM325 is therefore inhibition of Ubiquitin Specific Protease 20 (USP20, Accession NM_006676). Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with USP20. LOC144811

(Accession XM_096681) is another VGAM325 host target gene. LOC144811 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC144811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC144811 BINDING SITE, designated SEQ ID:40455, to the nucleotide sequence of VGAM325 RNA, herein designated VGAM RNA, also designated SEQ ID:3036.

[17127] Another function of VGAM325 is therefore inhibition of LOC144811 (Accession XM_096681). Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC144811. LOC92235 (Accession XM_043739) is another VGAM325 host target gene. LOC92235 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92235, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92235 BINDING SITE, designated SEQ ID:34012, to the nucleotide sequence of VGAM325 RNA, herein designated

VGAM RNA, also designated SEQ ID:3036.

[17128] Another function of VGAM325 is therefore inhibition of LOC92235 (Accession XM_043739). Accordingly, utilities of VGAM325 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92235. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 326 (VGAM326) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17129] VGAM326 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM326 was detected is described hereinabove with reference to Figs. 1–8.

[17130] VGAM326 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17131] VGAM326 gene encodes a VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other

miRNA genes, and unlike most ordinary genes, VGAM326 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM326 precursor RNA is designated SEQ ID:312, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:312 is located at position 66122 relative to the genome of Rabbit Fibroma Virus.

[17132] VGAM326 precursor RNA folds onto itself, forming VGAM326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17133] An enzyme complex designated DICER COMPLEX, `dices` the VGAM326 folded precursor RNA into VGAM326 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex

comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM326 RNA is designated SEQ ID:3037, and is provided hereinbelow with reference to the sequence listing part.

[17134] VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM326 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17135] VGAM326 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM326 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and

BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM326 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17136] The complementary binding of VGAM326 RNA, herein designated VGAM RNA, to host target binding sites on VGAM326 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM326 host target RNA into VGAM326 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17137] It is appreciated that VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM326 host target genes. The mRNA of

each one of this plurality of VGAM326 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM326 RNA, herein designated VGAM RNA, and which when bound by VGAM326 RNA causes inhibition of translation of respective one or more VGAM326 host target proteins.

[17138] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM326 gene, herein designated VGAM GENE, on one or more VGAM326 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science

294,779 (2001)).

[17139] It is yet further appreciated that a function of VGAM326 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM326 correlate with, and may be deduced from, the identity of the host target genes which VGAM326 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17140] Nucleotide sequences of the VGAM326 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM326 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM326 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM326 are further described hereinbelow with reference to Table 1.

[17141] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM326 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM326 RNA, herein desig-

nated VGAM RNA, are described hereinbelow with reference to Table 2.

[17142] As mentioned hereinabove with reference to Fig. 1, a function of VGAM326 gene, herein designated VGAM is inhibition of expression of VGAM326 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM326 correlate with, and may be deduced from, the identity of the target genes which VGAM326 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17143] Activin A Receptor, Type I (ACVR1, Accession NM_001105) is a VGAM326 host target gene. ACVR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ACVR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ACVR1 BINDING SITE, designated SEQ ID:6764, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17144] A function of VGAM326 is therefore inhibition of Activin A Receptor, Type I (ACVR1, Accession NM_001105), a gene which Activin receptor-like kinase; similar to activin, TGF-

beta, and *C. elegans* daf-1 receptors. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ACVR1. The function of ACVR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM217. BTG Family, Member 2 (BTG2, Accession NM_006763) is another VGAM326 host target gene. BTG2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTG2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTG2 BINDING SITE, designated SEQ ID:13630, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17145] Another function of VGAM326 is therefore inhibition of BTG Family, Member 2 (BTG2, Accession NM_006763). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTG2. Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM_000391) is another VGAM326 host target gene.

CLN2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CLN2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CLN2 BINDING SITE, designated SEQ ID:5968, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17146] Another function of VGAM326 is therefore inhibition of Ceroid-lipofuscinosis, Neuronal 2, Late Infantile (Jansky-Bielschowsky disease) (CLN2, Accession NM_000391). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CLN2. Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729) is another VGAM326 host target gene. DIAPH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DIAPH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DIAPH2 BINDING SITE, designated SEQ ID:13563, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM

RNA, also designated SEQ ID:3037.

[17147] Another function of VGAM326 is therefore inhibition of Diaphanous Homolog 2 (Drosophila) (DIAPH2, Accession NM_006729), a gene which may affect in oogenesis. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DIAPH2. The function of DIAPH2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM129. Forkhead Box D2 (FOXD2, Accession NM_004474) is another VGAM326 host target gene. FOXD2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FOXD2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FOXD2 BINDING SITE, designated SEQ ID:10789, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17148] Another function of VGAM326 is therefore inhibition of Forkhead Box D2 (FOXD2, Accession NM_004474). Accordingly, utilities of VGAM326 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with FOXD2. Glutaminase (GLS, Accession NM_014905) is another VGAM326 host target gene. GLS BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GLS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GLS BINDING SITE, designated SEQ ID:17106, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17149] Another function of VGAM326 is therefore inhibition of Glutaminase (GLS, Accession NM_014905). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GLS. Glycoprotein M6A (GPM6A, Accession NM_005277) is another VGAM326 host target gene. GPM6A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by GPM6A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GPM6A BINDING SITE, designated SEQ

ID:11781, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17150] Another function of VGAM326 is therefore inhibition of Glycoprotein M6A (GPM6A, Accession NM_005277), a gene which may play a role in neuronal development. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GPM6A. The function of GPM6A has been established by previous studies. Yan et al. (1993) used monoclonal antibodies raised against antigens in mouse brain fractions to isolate 2 related cDNAs from an expression library. The cDNAs, which they designated M6a and M6b (OMIM Ref. No. 300051), are highly similar to the myelin proteolipid protein (OMIM Ref. No. 300401) and are expressed during early development of the mouse central nervous system (CNS). Olinsky et al. (1996) found that the M6a gene (GPM6A) is expressed only in neurons. They obtained partial human genomic and cDNA clones for M6a and mapped the gene to 4q34 by fluorescence in situ hybridization. M6, a cell surface glycoprotein mainly expressed on neurons in the murine CNS, plays significant roles in neural cell adhesion and some aspects of neurite

growth (Lagenaur et al., 1992). Shimizu et al. (1996) isolated a human cDNA that is highly homologous to the murine gene, symbolized Gpm6, that encodes M6. The human gene, GPM6A, contains an open reading frame of 834 nucleotides encoding a peptide of 278 amino acids. Northern blot analysis revealed specific expression in human brain. By radiation hybrid mapping, Shimizu et al. (1996) assigned the GPM6A gene to 4q33–q34.

[17151] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17152] Shimizu, F.; Watanabe, T. K.; Fujiwara, T.; Takahashi, E.; Nakamura, Y.; Maekawa, H. : Isolation and mapping of the human glycoprotein M6 gene (GPM6A) to 4q33–to–q34. Cytogenet. Cell Genet. 74: 138–139, 1996. ; and

[17153] Yan, Y.; Lagenaur, C.; Narayanan, V. : Molecular cloning of M6: identification of a PLP/DM20 gene family. Neuron 11: 423–431, 1993.

[17154] Further studies establishing the function and utilities of GPM6A are found in John Hopkins OMIM database record ID 601275, and in cited publications numbered 986 and 9863 listed in the bibliography section hereinbelow, which are also hereby incorporated by refer–

ence.5-hydroxytryptamine (serotonin) Receptor 6 (HTR6, Accession NM_000871) is another VGAM326 host target gene. HTR6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by HTR6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HTR6 BINDING SITE, designated SEQ ID:6549, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17155] Another function of VGAM326 is therefore inhibition of 5-hydroxytryptamine (serotonin) Receptor 6 (HTR6, Accession NM_000871), a gene which stimulates adenylate cyclase. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HTR6. The function of HTR6 has been established by previous studies. Rees et al. (1994) identified a serotonin receptor subtype, HTR5A, that appeared to be expressed uniquely in the central nervous system. Schanen et al. (1996) used PCR analysis of somatic cell hybrid panels and a collection of chromosome 7-specific YAC clones to map HTR5A to 7q36.1.

[17156] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [17157] Rees, S.; den Daas, I.; Foord, S.; Goodson, S.; Bull, D.; Kilpatrick, G.; Lee, M. : Cloning and characterisation of the human 5-HT5A serotonin receptor. FEBS Lett. 355: 242-246, 1994. ; and
- [17158] Schanen, N. C.; Scherer, S. W.; Tsui, L.-C.; Francke, U. : Assignment of the 5-hydroxytryptamine (serotonin) receptor 5A gene (HTR5A) to human chromosome band 7q36.1. Cytogenet. Cell Ge.
- [17159] Further studies establishing the function and utilities of HTR6 are found in John Hopkins OMIM database record ID 601109, and in cited publications numbered 10246 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Interleukin 12 Receptor, Beta 2 (IL12RB2, Accession NM_001559) is another VGAM326 host target gene. IL12RB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IL12RB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IL12RB2 BINDING SITE, designated SEQ ID:7280, to the nucleotide

sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17160] Another function of VGAM326 is therefore inhibition of Interleukin 12 Receptor, Beta 2 (IL12RB2, Accession NM_001559), a gene which is involved in il-12 transduction. binds to il-12 with a low affinity. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IL12RB2. The function of IL12RB2 has been established by previous studies. Chua et al. (1994) and Presky et al. (1996) identified 2 subunits of the interleukin-12 (IL12; 161560) receptor complex designated beta-1 (OMIM Ref. No. 601604) and beta-2, respectively. Presky et al. (1996) identified IL12RB2 cDNA from a human phytohemagglutinin-activated lymphoblast library. It is an 862-amino acid type I transmembrane protein with a 595-amino acid-long extracellular domain and a cytoplasmic tail of 216 amino acids that contains 3 tyrosine residues. A cDNA encoding the mouse homolog was also isolated. The human and mouse proteins show 68% amino acid sequence identity. When expressed in COS-7 cells, IL12RB2 exists as a disulfide-linked oligomer with an apparent monomeric molecular weight of 130 kD. Functional stud-

ies indicated that high affinity IL12R is composed of at least 2 beta-type cytokine receptor subunits, each independently exhibiting low affinity for IL12. IL12RB1 is constitutively expressed on both Th1 and Th2 lymphocytes. IL12RB2 is expressed more strongly on Th1 cells, however, and can be induced by antigen receptor triggering or by IL12 and alpha-interferon (IFN α ; 147660). Using RT-PCR analysis, Kim et al. (2001) showed that IL12RB2 expression was high in lesions of tuberculoid (i.e., *M. leprae*-resistant) leprosy (see OMIM Ref. No. 246300) patients but not in lesions of lepromatous (i.e., low-resistance) patients. IL12RB1 expression was similar in both groups. Flow cytometric analysis demonstrated that tuberculoid patient T cells responded with increased expression of IL12RB1 and IL12RB2 to *M. leprae* antigen stimulation, whereas lepromatous patients upregulated expression of IL12RB1 but not IL12RB2. EMSA, supershift, and Western blot analyses indicated that IL12 stimulation induced STAT4 phosphorylation and STAT4-DNA binding in tuberculoid but not lepromatous patients. The defect in lepromatous patients was specific to *M. leprae* in that they upregulated both IL12RB1 and IL12RB2 in response to *M. tuberculosis* and activated the STAT4 pathway. ELISA anal-

ysis showed that production of IFNG (OMIM Ref. No. 147570) correlated with IL12RB2 expression in the leprosy patients. Kim et al. (2001) proposed that the Th response to antigen determines IL12RB2 expression and function in the generation of cell-mediated immunity to microbial infection

[17161] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17162] Presky, D. H.; Yang, H.; Minetti, L. J.; Chua, A. O.; Nabavi, N.; Wu, C.-Y.; Gately, M. K.; Gubler, U. : A functional interleukin 12 receptor complex is composed of two beta-type cytokine receptor subunits. Proc. Nat. Acad. Sci. 93: 14002-14007, 1996. ; and

[17163] Kim, J.; Uyemura, K.; Van Dyke, M. K.; Legaspi, A. J.; Rea, T. H.; Shuai, K.; Modlin, R. L. : A role for IL-12 receptor expression and signal transduction in host defense in leprosy. J.

[17164] Further studies establishing the function and utilities of IL12RB2 are found in John Hopkins OMIM database record ID 601642, and in cited publications numbered 4894, 6685-668 and 8854-8855 listed in the bibliography section hereinbelow, which are also hereby incorporated by

reference. Leukocyte-associated Ig-like Receptor 1 (LAIR1, Accession NM_002287) is another VGAM326 host target gene. LAIR1 BINDING SITE1 and LAIR1 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LAIR1, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LAIR1 BINDING SITE1 and LAIR1 BINDING SITE2, designated SEQ ID:8068 and SEQ ID:22322 respectively, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17165] Another function of VGAM326 is therefore inhibition of Leukocyte-associated Ig-like Receptor 1 (LAIR1, Accession NM_002287), a gene which Inhibitory receptor that represses cytotoxicity of natural killer cells and of T cell clones that lack CD28; contains an immunoglobulin-like domain. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LAIR1. The function of LAIR1 has been established by previous studies. Natural killer (NK) cells are a subpopulation of lymphocytes capable of lysing transformed and virus-infected cells without appar-

ent presensitization. Inhibitory receptors present on NK cells prevent excessive inflammatory responses and autoimmunity by binding major histocompatibility complex (MHC) expressed on target cells, resulting in the NK cells selectively killing only targets that lack MHC on their surface. Two families of human NK cell inhibitory receptors are the killer cell inhibitory receptors of the immunoglobulin superfamily and the NKG2 receptors (e.g., KLRC1; 161555) of the C-type lectin superfamily. All of these inhibitory receptors possess cytoplasmic tails with immune receptor tyrosine-based inhibitory motifs (ITIMs), which bind to the SH2 domain of certain phosphatases upon phosphorylation, leading to the downregulation of cell activation. To identify molecules involved in the negative signaling of NK cells, Meyaard et al. (1997) immunized mice with a human NK cell clone and screened antibodies for the capacity to inhibit NK cell-mediated lysis of Fc receptor (FcR)-bearing targets. They isolated a monoclonal antibody that recognized LAIR1. They found that FcR crosslinking of LAIR1 was required to deliver the negative signal and that it led to inhibition of cytotoxicity even in the presence of strong positive signals. Both the SH2-containing tyrosine phosphatases SHP1 (PTPN6;

176883) and SHP2 (PTPN11; 176876) associated with tyrosine-phosphorylated LAIR1. LAIR1 does not appear to recognize class I human leukocyte antigens (HLAs). LAIR1 was expressed on the majority of human peripheral blood mononuclear leukocytes examined Using flow cytometry to screen cell lines with a LAIR1 fusion protein, Meyaard et al. (2001) identified a LAIR1 ligand on colon carcinoma cell lines. By expression cloning from a colon carcinoma cDNA library, they showed that the LAIR1 ligand is identical to EPCAM (TACSTD1; 185535). EPCAM also binds LAIR2 (OMIM Ref. No. 602993), which is 84% homologous to LAIR1 in its Ig domain. Mutation analysis determined that EPCAM interacts with the LAIRs through its first EGF-like repeat. Flow cytometry and immunohistochemical analysis demonstrated LAIR1 expression in intestinal intraepithelial cells, in close proximity to cells expressing EPCAM. Meyaard et al. (2001) proposed that EPCAM, through its interaction with the LAIR1 inhibitory receptor, is involved in preventing excessive inflammatory responses in regions, such as intestine, with high antigen exposure

[17166] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [17167] Sathish, J. G.; Johnson, K. G.; Fuller, K. J.; LeRoy, F. G.; Meyaard, L.; Sims, M. J.; Matthews, R. J. : Constitutive association of SHP-1 with leukocyte-associated Ig-like receptor-1 in human T cells. J. Immun. 166: 1763-1770, 2001. ; and
- [17168] Xu, M.; Zhao, R.; Zhao, Z. J. : Identification and characterization of leukocyte-associated Ig-like receptor-1 as a major anchor protein of tyrosine phosphatase SHP-1 in hematopoietic c.
- [17169] Further studies establishing the function and utilities of LAIR1 are found in John Hopkins OMIM database record ID 602992, and in cited publications numbered 689, 540 and 5407-5408 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Phospholipase A2 Receptor 1, 180kDa (PLA2R1, Accession NM_007366) is another VGAM326 host target gene. PLA2R1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PLA2R1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PLA2R1 BINDING SITE, designated SEQ

ID:14295, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17170] Another function of VGAM326 is therefore inhibition of Phospholipase A2 Receptor 1, 180kDa (PLA2R1, Accession NM_007366). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PLA2R1. Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011) is another VGAM326 host target gene. SOCS5 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SOCS5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SOCS5 BINDING SITE, designated SEQ ID:15225, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17171] Another function of VGAM326 is therefore inhibition of Suppressor of Cytokine Signaling 5 (SOCS5, Accession NM_014011). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SOCS5. Transcription Fac-

tor-like 4 (TCFL4, Accession XM_032817) is another VGAM326 host target gene. TCFL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TCFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TCFL4 BINDING SITE, designated SEQ ID:31769, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17172] Another function of VGAM326 is therefore inhibition of Transcription Factor-like 4 (TCFL4, Accession XM_032817), a gene which interacts with Mad and represses transcription by recruiting the Sin3A-histone deacetylase corepressor complex. Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TCFL4. The function of TCFL4 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM172. Activity-dependent Neuroprotector (ADNP, Accession NM_015339) is another VGAM326 host target gene. ADNP BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by ADNP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ADNP BINDING SITE, designated SEQ ID:17647, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17173] Another function of VGAM326 is therefore inhibition of Activity-dependent Neuroprotector (ADNP, Accession NM_015339). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ADNP. Ac-like Transposable Element (ALTE, Accession NM_004729) is another VGAM326 host target gene. ALTE BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALTE, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALTE BINDING SITE, designated SEQ ID:11105, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17174] Another function of VGAM326 is therefore inhibition of

Ac-like Transposable Element (ALTE, Accession NM_004729). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALTE. Centaurin, Alpha 2 (CENTA2, Accession NM_018404) is another VGAM326 host target gene. CENTA2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENTA2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENTA2 BINDING SITE, designated SEQ ID:20444, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17175] Another function of VGAM326 is therefore inhibition of Centaurin, Alpha 2 (CENTA2, Accession NM_018404). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CENTA2. DKFZP434B172 (Accession XM_046264) is another VGAM326 host target gene. DKFZP434B172 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434B172, corresponding to a HOST TARGET binding

site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434B172 BINDING SITE, designated SEQ ID:34702, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17176] Another function of VGAM326 is therefore inhibition of DKFZP434B172 (Accession XM_046264). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434B172. DKFZp586G0123 (Accession XM_170914) is another VGAM326 host target gene. DKFZp586G0123 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by DKFZp586G0123, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZp586G0123 BINDING SITE, designated SEQ ID:45693, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17177] Another function of VGAM326 is therefore inhibition of DKFZp586G0123 (Accession XM_170914). Accordingly,

utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZp586G0123. Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665) is another VGAM326 host target gene. EVI5 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by EVI5, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EVI5 BINDING SITE, designated SEQ ID:12213, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17178] Another function of VGAM326 is therefore inhibition of Ecotropic Viral Integration Site 5 (EVI5, Accession NM_005665). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EVI5. FLJ14280 (Accession NM_024886) is another VGAM326 host target gene. FLJ14280 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ14280, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14280 BINDING SITE, designated SEQ ID:24340, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17179] Another function of VGAM326 is therefore inhibition of FLJ14280 (Accession NM_024886). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14280. FLJ22127 (Accession NM_022775) is another VGAM326 host target gene. FLJ22127 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ22127, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ22127 BINDING SITE, designated SEQ ID:23042, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17180] Another function of VGAM326 is therefore inhibition of FLJ22127 (Accession NM_022775). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ22127.

FLJ30681 (Accession XM_166291) is another VGAM326 host target gene. FLJ30681 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ30681, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ30681 BINDING SITE, designated SEQ ID:44107, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17181] Another function of VGAM326 is therefore inhibition of FLJ30681 (Accession XM_166291). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ30681. KIAA1831 (Accession XM_033366) is another VGAM326 host target gene. KIAA1831 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1831 BINDING SITE, designated SEQ ID:31902, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3037.

[17182] Another function of VGAM326 is therefore inhibition of KIAA1831 (Accession XM_033366). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1831. KIAA1854 (Accession XM_049884) is another VGAM326 host target gene. KIAA1854 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1854 BINDING SITE, designated SEQ ID:35534, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17183] Another function of VGAM326 is therefore inhibition of KIAA1854 (Accession XM_049884). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1854. LBP-9 (Accession NM_014553) is another VGAM326 host target gene. LBP-9 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LBP-9, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBP-9 BINDING SITE, designated SEQ ID:15875, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17184] Another function of VGAM326 is therefore inhibition of LBP-9 (Accession NM_014553). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LBP-9. Microtubule-actin Crosslinking Factor 1 (MACF1, Accession NM_012090) is another VGAM326 host target gene. MACF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MACF1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MACF1 BINDING SITE, designated SEQ ID:14380, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17185] Another function of VGAM326 is therefore inhibition of Microtubule-actin Crosslinking Factor 1 (MACF1, Acces-

sion NM_012090). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MACF1. PR Domain Containing 15 (PRDM15, Accession XM_029600) is another VGAM326 host target gene. PRDM15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRDM15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRDM15 BINDING SITE, designated SEQ ID:30916, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17186] Another function of VGAM326 is therefore inhibition of PR Domain Containing 15 (PRDM15, Accession XM_029600). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRDM15. PRO1386 (Accession NM_031269) is another VGAM326 host target gene. PRO1386 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO1386, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of PRO1386 BINDING SITE, designated SEQ ID:25288, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17187] Another function of VGAM326 is therefore inhibition of PRO1386 (Accession NM_031269). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1386. SCDGF-B (Accession NM_025208) is another VGAM326 host target gene. SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by SCDGF-B, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCDGF-B BINDING SITE1 and SCDGF-B BINDING SITE2, designated SEQ ID:24880 and SEQ ID:26982 respectively, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17188] Another function of VGAM326 is therefore inhibition of SCDGF-B (Accession NM_025208). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of

diseases and clinical conditions associated with SCDGF-B. TUSP (Accession NM_020245) is another VGAM326 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21522, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17189] Another function of VGAM326 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. LOC124222 (Accession XM_058784) is another VGAM326 host target gene. LOC124222 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC124222, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC124222 BINDING SITE, designated SEQ ID:36742, to the nucleotide se-

quence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17190] Another function of VGAM326 is therefore inhibition of LOC124222 (Accession XM_058784). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC124222. LOC139422 (Accession XM_066687) is another VGAM326 host target gene. LOC139422 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC139422, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139422 BINDING SITE, designated SEQ ID:37343, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17191] Another function of VGAM326 is therefore inhibition of LOC139422 (Accession XM_066687). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139422. LOC145871 (Accession XM_096897) is another VGAM326 host target gene. LOC145871 BINDING SITE is HOST TARGET binding site found in the 5` un-

translated region of mRNA encoded by LOC145871, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145871 BINDING SITE, designated SEQ ID:40621, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17192] Another function of VGAM326 is therefore inhibition of LOC145871 (Accession XM_096897). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145871. LOC148394 (Accession XM_097460) is another VGAM326 host target gene. LOC148394 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC148394, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148394 BINDING SITE, designated SEQ ID:40881, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17193] Another function of VGAM326 is therefore inhibition of LOC148394 (Accession XM_097460). Accordingly, utilities

of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148394. LOC148534 (Accession XM_086222) is another VGAM326 host target gene. LOC148534 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148534, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148534 BINDING SITE, designated SEQ ID:38548, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17194] Another function of VGAM326 is therefore inhibition of LOC148534 (Accession XM_086222). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148534. LOC148697 (Accession XM_086276) is another VGAM326 host target gene. LOC148697 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148697, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC148697 BINDING SITE, designated SEQ ID:38574, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17195] Another function of VGAM326 is therefore inhibition of LOC148697 (Accession XM_086276). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148697. LOC164714 (Accession XM_104657) is another VGAM326 host target gene. LOC164714 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164714 BINDING SITE, designated SEQ ID:42179, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17196] Another function of VGAM326 is therefore inhibition of LOC164714 (Accession XM_104657). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164714. LOC199858 (Accession XM_114040) is another VGAM326 host target gene. LOC199858 BINDING

SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC199858, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199858 BINDING SITE, designated SEQ ID:42640, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17197] Another function of VGAM326 is therefore inhibition of LOC199858 (Accession XM_114040). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199858. LOC200982 (Accession XM_117305) is another VGAM326 host target gene. LOC200982 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200982, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200982 BINDING SITE, designated SEQ ID:43377, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17198] Another function of VGAM326 is therefore inhibition of

LOC200982 (Accession XM_117305). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200982. LOC255714 (Accession XM_172861) is another VGAM326 host target gene. LOC255714 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC255714, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC255714 BINDING SITE, designated SEQ ID:46141, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17199] Another function of VGAM326 is therefore inhibition of LOC255714 (Accession XM_172861). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC255714. LOC57228 (Accession NM_020467) is another VGAM326 host target gene. LOC57228 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC57228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illus-

trates the complementarity of the nucleotide sequences of LOC57228 BINDING SITE, designated SEQ ID:21707, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17200] Another function of VGAM326 is therefore inhibition of LOC57228 (Accession NM_020467). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC57228. LOC91531 (Accession XM_038998) is another VGAM326 host target gene. LOC91531 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC91531, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91531 BINDING SITE, designated SEQ ID:32973, to the nucleotide sequence of VGAM326 RNA, herein designated VGAM RNA, also designated SEQ ID:3037.

[17201] Another function of VGAM326 is therefore inhibition of LOC91531 (Accession XM_038998). Accordingly, utilities of VGAM326 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91531. Fig. 1 further provides a conceptual descrip-

tion of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 327 (VGAM327) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17202] VGAM327 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM327 was detected is described hereinabove with reference to Figs. 1–8.

[17203] VGAM327 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17204] VGAM327 gene encodes a VGAM327 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM327 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM327 precursor RNA is designated SEQ ID:313, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:313 is

located at position 66535 relative to the genome of Rabbit Fibroma Virus.

[17205] VGAM327 precursor RNA folds onto itself, forming VGAM327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17206] An enzyme complex designated DICER COMPLEX, `dices` the VGAM327 folded precursor RNA into VGAM327 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide sequence of VGAM327 RNA is designated SEQ ID:3038, and is provided hereinbelow with reference to the sequence listing part.

[17207] VGAM327 host target gene, herein designated VGAM

HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM327 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5' UTR, PROTEIN CODING and 3' UTR respectively.

[17208] VGAM327 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM327 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM327 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM327 host target RNA,

herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3' UTR region, this is meant as an example only – these host target binding sites may be located in the 3' UTR region, the 5' UTR region, or in both 3' UTR and 5' UTR regions.

[17209] The complementary binding of VGAM327 RNA, herein designated VGAM RNA, to host target binding sites on VGAM327 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM327 host target RNA into VGAM327 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17210] It is appreciated that VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM327 host target genes. The mRNA of each one of this plurality of VGAM327 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM327 RNA, herein designated VGAM RNA, and which when bound by VGAM327 RNA causes inhibition of translation of respective one or more VGAM327

host target proteins.

[17211] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM327 gene, herein designated VGAM GENE, on one or more VGAM327 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17212] It is yet further appreciated that a function of VGAM327 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Spe-

cific functions, and accordingly utilities, of VGAM327 correlate with, and may be deduced from, the identity of the host target genes which VGAM327 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17213] Nucleotide sequences of the VGAM327 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM327 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM327 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM327 are further described hereinbelow with reference to Table 1.

[17214] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM327 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM327 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17215] As mentioned hereinabove with reference to Fig. 1, a function of VGAM327 gene, herein designated VGAM is inhibition of expression of VGAM327 target genes. It is appreciated that specific functions, and accordingly utili-

ties, of VGAM327 correlate with, and may be deduced from, the identity of the target genes which VGAM327 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17216] Endometrial Bleeding Associated Factor (left-right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM_037302) is a VGAM327 host target gene. EBAF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EBAF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EBAF BINDING SITE, designated SEQ ID:32609, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17217] A function of VGAM327 is therefore inhibition of Endometrial Bleeding Associated Factor (left-right determination, factor A; transforming growth factor beta superfamily) (EBAF, Accession XM_037302), a gene which LEFT-RIGHT AXIS MALFORMATIONS. Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EBAF. The function

of EBAF and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM93.N-ethylmaleimide-sensitive Factor Attachment Protein, Beta (NAPB, Accession XM_046652) is another VGAM327 host target gene. NAPB BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NAPB, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NAPB BINDING SITE, designated SEQ ID:34766, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17218] Another function of VGAM327 is therefore inhibition of N-ethylmaleimide-sensitive Factor Attachment Protein, Beta (NAPB, Accession XM_046652). Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NAPB. Protein Tyrosine Phosphatase, Non-receptor Type 1 (PTPN1, Accession NM_002827) is another VGAM327 host target gene. PTPN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded

by PTPN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTPN1 BINDING SITE, designated SEQ ID:8701, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17219] Another function of VGAM327 is therefore inhibition of Protein Tyrosine Phosphatase, Non-receptor Type 1 (PTPN1, Accession NM_002827), a gene which is a non-receptor type 1 protein tyrosine phosphatase and inhibits insulin signaling. Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PTPN1. The function of PTPN1 has been established by previous studies. PTP1B inhibits insulin signaling and, when overexpressed, plays a role in insulin resistance (Ahmad et al., 1997). In the 3-prime untranslated region of the PTP1B gene, Di Paola et al. (2002) identified a 1484insG variation (176885.0001) that, in 2 different populations, was associated with several features of insulin resistance. Similar data were obtained in a family-based association study by use of sib pairs discordant for genotype (Gu et al., 2000).

Subjects carrying the 1484insG variant showed PTP1B mRNA overexpression in skeletal muscle. PTP1B mRNA stability was significantly higher in human embryonic kidney cells transfected with 1484insG PTP1B as compared with those transfected with wildtype PTP1B. The data indicated that the 1484insG allele causes PTP1B overexpression and plays a role in insulin resistance. Therefore, individuals carrying the 1484insG variant might particularly benefit from PTP1B inhibitors in the treatment of insulin resistance (Kennedy and Ramachandran, 2000). Animal model experiments lend further support to the function of PTPN1. Elchebly et al. (1999) generated PTP1B-deficient mice by targeted disruption of the mouse homolog of the PTP1B gene. Mice were phenotypically and pathologically normal and had normal life span. In the fed state, homozygous mutant mice had slightly lower blood glucose concentrations, and half the circulating insulin concentrations, of wildtype littermates. The enhanced insulin sensitivity of PTP1B-deficient mice was also evident in glucose- and insulin-tolerance tests. After insulin injection, deficient mice showed increased phosphorylation of the insulin receptor in liver and muscle tissue compared to wildtype mice. On a high-fat diet, PTP1B-deficient mice

were resistant to weight gain and remained insulin sensitive, while wildtype mice rapidly gained weight and became insulin resistant. These results suggested a major role for PTP1B in modulation of insulin sensitivity and fuel metabolism. The authors proposed PTP1B as a potential therapeutic target for the treatment of type 2 diabetes and obesity.

[17220] It is appreciated that the abovementioned animal model for PTPN1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17221] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17222] Elchebly, M.; Payette, P.; Michaliszyn, E.; Cromlish, W.; Collins, S.; Loy, A. L.; Normandin, D.; Cheng, A.; Himms-Hagen, J.; Chan, C.-C.; Ramachandran, C.; Gresser, M. J.; Tremblay, M. L.; Kennedy, B. P. : Increased insulin sensitivity and obesity resistance in mice lacking the protein tyrosine phosphatase-1B gene. Science 283: 1544-1548, 1999. ; and

[17223] Di Paola, R.; Frittitta, L.; Miscio, G.; Bozzali, M.; Baratta, R.; Centra, M.; Spampinato, D.; Santagati, M. G.; Ercolino, T.;

Cisternino, C.; Soccio, T. Mastroianno, S.; Tassi, V.; Alm.

[17224] Further studies establishing the function and utilities of PTPN1 are found in John Hopkins OMIM database record ID 176885, and in cited publications numbered 10896–10899, 10698–10575, 10890, 1057 and 10579 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. KIAA0960 (Accession XM_166543) is another VGAM327 host target gene. KIAA0960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0960 BINDING SITE, designated SEQ ID:44514, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17225] Another function of VGAM327 is therefore inhibition of KIAA0960 (Accession XM_166543). Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0960. LOC158187 (Accession XM_098892) is another VGAM327 host target gene. LOC158187 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC158187, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC158187 BINDING SITE, designated SEQ ID:41920, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17226] Another function of VGAM327 is therefore inhibition of LOC158187 (Accession XM_098892). Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC158187. LOC90620 (Accession XM_032986) is another VGAM327 host target gene. LOC90620 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC90620, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90620 BINDING SITE, designated SEQ ID:31805, to the nucleotide sequence of VGAM327 RNA, herein designated VGAM RNA, also designated SEQ ID:3038.

[17227] Another function of VGAM327 is therefore inhibition of

LOC90620 (Accession XM_032986). Accordingly, utilities of VGAM327 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90620. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 328 (VGAM328) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17228] VGAM328 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM328 was detected is described hereinabove with reference to Figs. 1–8.

[17229] VGAM328 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17230] VGAM328 gene encodes a VGAM328 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM328 precursor RNA does not encode a protein. A nucleotide

sequence identical or highly similar to the nucleotide sequence of VGAM328 precursor RNA is designated SEQ ID:314, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:314 is located at position 68066 relative to the genome of Rabbit Fibroma Virus.

[17231] VGAM328 precursor RNA folds onto itself, forming VGAM328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17232] An enzyme complex designated DICER COMPLEX, `dices` the VGAM328 folded precursor RNA into VGAM328 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 80%) nucleotide se-

quence of VGAM328 RNA is designated SEQ ID:3039, and is provided hereinbelow with reference to the sequence listing part.

[17233] VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM328 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[17234] VGAM328 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM328 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is

meant as an illustration only, and is not meant to be limiting – VGAM328 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[17235] The complementary binding of VGAM328 RNA, herein designated VGAM RNA, to host target binding sites on VGAM328 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM328 host target RNA into VGAM328 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17236] It is appreciated that VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM328 host target genes. The mRNA of each one of this plurality of VGAM328 host target genes comprises one or more host target binding sites, each

having a nucleotide sequence which is at least partly complementary to VGAM328 RNA, herein designated VGAM RNA, and which when bound by VGAM328 RNA causes inhibition of translation of respective one or more VGAM328 host target proteins.

[17237] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM328 gene, herein designated VGAM GENE, on one or more VGAM328 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17238] It is yet further appreciated that a function of VGAM328 is

inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM328 correlate with, and may be deduced from, the identity of the host target genes which VGAM328 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17239] Nucleotide sequences of the VGAM328 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM328 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM328 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM328 are further described hereinbelow with reference to Table 1.

[17240] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM328 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM328 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17241] As mentioned hereinabove with reference to Fig. 1, a function of VGAM328 gene, herein designated VGAM is inhibition of expression of VGAM328 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM328 correlate with, and may be deduced from, the identity of the target genes which VGAM328 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17242] Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502) is a VGAM328 host target gene. CX3CR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CX3CR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CX3CR1 BINDING SITE, designated SEQ ID:34973, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17243] A function of VGAM328 is therefore inhibition of Chemokine (C-X3-C motif) Receptor 1 (CX3CR1, Accession XM_047502), a gene which mediates both the adhesive and migratory functions of fractalkine. Accordingly,

utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CX3CR1. The function of CX3CR1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM25. Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM_000118) is another VGAM328 host target gene. ENG BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ENG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ENG BINDING SITE, designated SEQ ID:5589, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17244] Another function of VGAM328 is therefore inhibition of Endoglin (Osler–Rendu–Weber syndrome 1) (ENG, Accession NM_000118). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ENG. Myeloid/lymphoid Or Mixed–lineage Leukemia (trithorax homolog, *Drosophila*); Translocated To, 3 (MLLT3, Accession

NM_004529) is another VGAM328 host target gene.

MLLT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MLLT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MLLT3 BINDING SITE, designated SEQ ID:10866, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17245] Another function of VGAM328 is therefore inhibition of Myeloid/lymphoid Or Mixed-lineage Leukemia (trithorax homolog, Drosophila); Translocated To, 3 (MLLT3, Accession NM_004529), a gene which is Serine and proline rich protein. Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MLLT3. The function of MLLT3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM67. Transforming Growth Factor, Alpha (TGFA, Accession NM_003236) is another VGAM328 host target gene. TGFA BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by TGFA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TGFA BINDING SITE, designated SEQ ID:9230, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17246] Another function of VGAM328 is therefore inhibition of Transforming Growth Factor, Alpha (TGFA, Accession NM_003236), a gene which is able to bind to the egf receptor and to act synergistically with tgfbeta to promote anchorage-independent cell proliferation in soft agar. Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TGFA. The function of TGFA has been established by previous studies. Ellis et al. (1987) presented evidence that TGFA plays a role in certain paraneoplastic manifestations of melanoma: the sign of Leser-Trelat (the sudden appearance of, or increase in the number and size of, seborrheic keratoses), acanthosis nigricans, and eruptive acrochordons (sudden onset of multiple skin tags). Fernandez-Larrea et al. (1999) used the 2-hybrid screen to identify pro-TGF-alpha cytoplasmic domain-binding

proteins, which they referred to as TACIPs (pro-TGF- α cytoplasmic domain-interacting proteins), involved in the trafficking of pro-TGF- α . They cloned 2 such proteins, which they designated TACIP1 (OMIM Ref. No. 601017) and TACIP18 (OMIM Ref. No. 602217). The circadian clock in the suprachiasmatic nucleus is thought to drive daily rhythms of behavior by secreting factors that act locally within the hypothalamus. In a systematic screen, Kramer et al. (2001) identified TGFA as a likely suprachiasmatic nucleus inhibitor of locomotion. TGFA is expressed rhythmically in the suprachiasmatic nucleus, and when infused into the third ventricle it reversibly inhibited locomotor activity and disrupted circadian sleep-wake cycles. These actions were mediated by EGF receptors on neurons in the hypothalamic subparaventricular zone. Mice with a hypomorphic EGF receptor mutation exhibited excessive daytime locomotor activity and failed to suppress activity when exposed to light. Kramer et al. (2001) concluded that their results implicate EGF receptor signaling in the daily control of locomotor activity. They identified a neural circuit in the hypothalamus that likely mediates the regulation of behavior both by the suprachiasmatic nucleus and the retina using TGFA and EGF re-

ceptors in the retinohypothalamic tract.

[17247] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17248] Fernandez-Larrea, J.; Merlos-Suarez, A.; Urena, J. M.; Baselga, J.; Arribas, J. : A role for a PDZ protein in the early secretory pathway for the targeting of proTGF- α to the cell surface. *Molec. Cell* 3: 423-433, 1999. ; and

[17249] Kramer, A.; Yang, F.-C.; Snodgrass, P.; Li, X.; Scammell, T. E.; Davis, F. C.; Weitz, C. J. : Regulation of daily locomotor activity and sleep by hypothalamic EGF receptor signaling. *S.*

[17250] Further studies establishing the function and utilities of TGFA are found in John Hopkins OMIM database record ID 190170, and in cited publications numbered 2705-2709, 37 and 2710-2712 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. FLJ10388 (Accession NM_018082) is another VGAM328 host target gene. FLJ10388 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10388, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the com-

plementarity of the nucleotide sequences of FLJ10388 BINDING SITE, designated SEQ ID:19841, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17251] Another function of VGAM328 is therefore inhibition of FLJ10388 (Accession NM_018082). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10388. HT002 (Accession NM_014066) is another VGAM328 host target gene. HT002 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HT002, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HT002 BINDING SITE, designated SEQ ID:15278, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17252] Another function of VGAM328 is therefore inhibition of HT002 (Accession NM_014066). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HT002. KIAA1831 (Accession XM_033366) is another VGAM328

host target gene. KIAA1831 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1831, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1831 BINDING SITE, designated SEQ ID:31901, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17253] Another function of VGAM328 is therefore inhibition of KIAA1831 (Accession XM_033366). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1831. MGC3251 (Accession NM_032016) is another VGAM328 host target gene. MGC3251 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MGC3251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC3251 BINDING SITE, designated SEQ ID:25730, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17254] Another function of VGAM328 is therefore inhibition of MGC3251 (Accession NM_032016). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC3251. LOC149134 (Accession XM_097594) is another VGAM328 host target gene. LOC149134 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC149134, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC149134 BINDING SITE, designated SEQ ID:40956, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17255] Another function of VGAM328 is therefore inhibition of LOC149134 (Accession XM_097594). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC149134. LOC220074 (Accession NM_145309) is another VGAM328 host target gene. LOC220074 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC220074, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC220074 BINDING SITE, designated SEQ ID:29824, to the nucleotide sequence of VGAM328 RNA, herein designated VGAM RNA, also designated SEQ ID:3039.

[17256] Another function of VGAM328 is therefore inhibition of LOC220074 (Accession NM_145309). Accordingly, utilities of VGAM328 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC220074. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 329 (VGAM329) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17257] VGAM329 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM329 was detected is described hereinabove with reference to Figs. 1–8.

[17258] VGAM329 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Rabbit Fibroma Virus. VGAM329 host target gene, herein designated VGAM

HOST TARGET GENE, is a human gene contained in the human genome.

[17259] VGAM329 gene encodes a VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM329 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM329 precursor RNA is designated SEQ ID:315, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:315 is located at position 76498 relative to the genome of Rabbit Fibroma Virus.

[17260] VGAM329 precursor RNA folds onto itself, forming VGAM329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17261] An enzyme complex designated DICER COMPLEX, `dices` the VGAM329 folded precursor RNA into VGAM329 RNA,

herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM329 RNA is designated SEQ ID:3040, and is provided hereinbelow with reference to the sequence listing part.

[17262] VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM329 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17263] VGAM329 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM329 RNA is an accurate or a

partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM329 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17264] The complementary binding of VGAM329 RNA, herein designated VGAM RNA, to host target binding sites on VGAM329 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM329 host target RNA into VGAM329 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target

protein is therefore outlined by a broken line.

[17265] It is appreciated that VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM329 host target genes. The mRNA of each one of this plurality of VGAM329 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM329 RNA, herein designated VGAM RNA, and which when bound by VGAM329 RNA causes inhibition of translation of respective one or more VGAM329 host target proteins.

[17266] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM329 gene, herein designated VGAM GENE, on one or more VGAM329 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate ex-

pression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17267] It is yet further appreciated that a function of VGAM329 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of viral infection by Rabbit Fibroma Virus. Specific functions, and accordingly utilities, of VGAM329 correlate with, and may be deduced from, the identity of the host target genes which VGAM329 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17268] Nucleotide sequences of the VGAM329 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM329 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM329 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM329 are further described hereinbelow with reference to Table 1.

[17269] Nucleotide sequences of host target binding sites, such as

BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM329 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM329 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17270] As mentioned hereinabove with reference to Fig. 1, a function of VGAM329 gene, herein designated VGAM is inhibition of expression of VGAM329 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM329 correlate with, and may be deduced from, the identity of the target genes which VGAM329 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17271] Adaptor-related Protein Complex 1, Gamma 1 Subunit (AP1G1, Accession NM_001128) is a VGAM329 host target gene. AP1G1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AP1G1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AP1G1 BINDING SITE, designated SEQ ID:6802, to the nucleotide sequence of VGAM329 RNA,

herein designated VGAM RNA, also designated SEQ ID:3040.

[17272] A function of VGAM329 is therefore inhibition of Adaptor-related Protein Complex 1, Gamma 1 Subunit (AP1G1, Accession NM_001128), a gene which promotes the formation of clathrin-coated pits and vesicles. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AP1G1. The function of AP1G1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM316. B-cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898) is another VGAM329 host target gene. BCL11B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCL11B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCL11B BINDING SITE, designated SEQ ID:23170, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17273] Another function of VGAM329 is therefore inhibition of B-

cell CLL/lymphoma 11B (zinc finger protein) (BCL11B, Accession NM_022898). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCL11B. Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719) is another VGAM329 host target gene. CACNA1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CACNA1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CACNA1C BINDING SITE, designated SEQ ID:6382, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17274] Another function of VGAM329 is therefore inhibition of Calcium Channel, Voltage-dependent, L Type, Alpha 1C Subunit (CACNA1C, Accession NM_000719), a gene which is alpha-1 subunit of DHP-sensitive calcium channels from cardiac muscle and the brain. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CACNA1C. The function of CACNA1C and its association with various

diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM182. Centrosomal Protein 2 (CEP2, Accession NM_007186) is another VGAM329 host target gene. CEP2 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by CEP2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CEP2 BINDING SITE, designated SEQ ID:14044, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17275] Another function of VGAM329 is therefore inhibition of Centrosomal Protein 2 (CEP2, Accession NM_007186), a gene which interacts with TC10 and CDC42. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CEP2. The function of CEP2 has been established by previous studies. Using a yeast 2-hybrid screen on a mouse embryo cDNA library with TC10 (OMIM Ref. No. 605857) as the bait, followed by EST database searching, Joberty et al. (1999) identified cDNAs encoding human and mouse BORG1 (CEP2), BORG2 (CEP3; 606133), BORG3

(CEP5), BORG4 (CEP4; 605468), and BORG5 (CEP1). Sequence analysis predicted that the 210-amino acid BORG1 protein contains a CRIB motif followed by a conserved 12-residue BORG homology-1 (BH1) domain in its N terminus; an 11-amino acid BH2 domain in its central region; and a 22-residue BH3 domain in its C terminus. Northern blot analysis detected ubiquitous but variable expression of 1.8- and 2.0-kb BORG1 transcripts, with high levels in heart and low levels in pancreas and liver. By binding analysis, Joberty et al. (1999) confirmed that BORG1 interacts with TC10 and CDC42. Immunofluorescence microscopy demonstrated cytoplasmic expression of BORG1. BORG1 expression caused no dramatic changes in cell shape and a reduced abundance of stress fibers. Coexpression of BORG1 with CDC42 resulted in cells showing a 'porcupine' phenotype characterized by an abundance of actin-filled spikes. By EST database searching with CEP1 as the probe, Hirsch et al. (2001) identified cDNAs encoding several CEPs, including CEP2. They referred to the BH2 and BH3 domains as CI and CII, respectively, and considered the BH1 domain to be part of an extended CRIB motif. Hirsch et al. (2001) proposed that these motifs are potential signaling domains. Fluores-

cence microscopy demonstrated cytoplasmic and membrane expression of CEP2 in keratinocytes, with notable localization in a perinuclear cytoplasmic compartment

[17276] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17277] Hirsch, D. S.; Pirone, D. M.; Burbelo, P. D. : A new family of Cdc42 effector proteins, CEPs, function in fibroblast and epithelial cell shape changes. J. Biol. Chem. 276: 875–883, 2001. ; and

[17278] Joberty, G.; Perlungher, R. R.; Macara, I. G. : The Borgs, a new family of Cdc42 and TC10 GTPase–interacting proteins. Molec. Cell. Biol. 19: 6585–6597, 1999.

[17279] Further studies establishing the function and utilities of CEP2 are found in John Hopkins OMIM database record ID 606132, and in cited publications numbered 6641–664 and 6471 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM_001271) is another VGAM329 host target gene. CHD2 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHD2, corresponding to a HOST TARGET binding site

such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHD2 BINDING SITE, designated SEQ ID:6937, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17280] Another function of VGAM329 is therefore inhibition of Chromodomain Helicase DNA Binding Protein 2 (CHD2, Accession NM_001271). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHD2. Disrupted In Schizophrenia 1 (DISC1, Accession NM_018662) is another VGAM329 host target gene. DISC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DISC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DISC1 BINDING SITE, designated SEQ ID:20737, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17281] Another function of VGAM329 is therefore inhibition of Disrupted In Schizophrenia 1 (DISC1, Accession

NM_018662), a gene which has globular N-terminal domain(s) and a helical C-terminal domain. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DISC1. The function of DISC1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM74. Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199) is another VGAM329 host target gene. EIF2C1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EIF2C1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EIF2C1 BINDING SITE, designated SEQ ID:14506, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17282] Another function of VGAM329 is therefore inhibition of Eukaryotic Translation Initiation Factor 2C, 1 (EIF2C1, Accession NM_012199), a gene which plays an important role in the eukaryotic peptide chain initiation process. Accordingly, utilities of VGAM329 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with EIF2C1. The function of EIF2C1 and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM118. Ficolin (collagen/fibrinogen domain containing) 3 (Hakata antigen) (FCN3, Accession NM_003665) is another VGAM329 host target gene. FCN3 BINDING SITE1 and FCN3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FCN3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FCN3 BINDING SITE1 and FCN3 BINDING SITE2, designated SEQ ID:9745 and SEQ ID:9746 respectively, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17283] Another function of VGAM329 is therefore inhibition of Ficolin (collagen/fibrinogen domain containing) 3 (Hakata antigen) (FCN3, Accession NM_003665). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FCN3. Matrix Metalloproteinase 14 (membrane-inserted)

(MMP14, Accession NM_004995) is another VGAM329 host target gene. MMP14 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MMP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MMP14 BINDING SITE, designated SEQ ID:11436, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17284] Another function of VGAM329 is therefore inhibition of Matrix Metalloproteinase 14 (membrane-inserted) (MMP14, Accession NM_004995). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MMP14. Membrane-spanning 4-domains, Subfamily A, Member 4 (MS4A4A, Accession NM_024021) is another VGAM329 host target gene. MS4A4A BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by MS4A4A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MS4A4A BINDING SITE,

designated SEQ ID:23450, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17285] Another function of VGAM329 is therefore inhibition of Membrane-spanning 4-domains, Subfamily A, Member 4 (MS4A4A, Accession NM_024021), a gene which binds to the fc region of immunoglobulins epsilon. high affinity receptor. initiating the allergic response. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MS4A4A. The function of MS4A4A has been established by previous studies. By EST database searching for homologs of CD20 (MS4A1; 112210), Ishibashi et al. (2001) isolated a cDNA encoding MS4A4A, which they called MS4A4. The deduced 205-amino acid protein has a conserved phosphorylation site at the intracellular loop. Northern blot analysis revealed weak expression in mouse colon and intestine but detected no expression in human tissues. Liang and Tedder (2001) also obtained a cDNA encoding MS4A4A. The predicted 220-amino acid protein is more than 40% identical to its mouse homologs. PCR analysis detected variable expression of MS4A4A in cDNA from multiple hemopoietic cell lines.

[17286] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17287] Ishibashi, K.; Suzuki, M.; Sasaki, S.; Imai, M. : Identification of a new multigene four-transmembrane family (MS4A) related to CD20, HTm4 and beta subunit of the high-affinity IgE receptor. Gene 264: 87-93, 2001. ; and

[17288] Liang, Y.; Tedder, T. F. : Identification of a CD20-, Fc-epsilon-RI-beta-related gene family: sixteen new MS4A family members expressed in human and mouse. Genomics 72: 119-127, 2001.

[17289] Further studies establishing the function and utilities of MS4A4A are found in John Hopkins OMIM database record ID 606547, and in cited publications numbered 4538-4539 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499) is another VGAM329 host target gene. NEO1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NEO1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NEO1 BIND-

ING SITE, designated SEQ ID:8320, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17290] Another function of VGAM329 is therefore inhibition of Neogenin Homolog 1 (chicken) (NEO1, Accession NM_002499), a gene which regulates the transition of undifferentiated proliferating cells to their differentiated state. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NEO1. The function of NEO1 has been established by previous studies. Vielmetter et al. (1994) identified a protein with roughly 50% amino acid identity to DCC (OMIM Ref. No. 120470); it showed a dynamic pattern of expression in the developing nervous system and gastrointestinal tract of the chicken. They termed this protein neogenin. Specifically, neogenin was induced in neural cells immediately before cell cycle withdrawal and terminal differentiation. Meyerhardt et al. (1997) cloned the human neogenin gene (symbolized NGN by them) and explored its possible role in cancer. They found cDNAs for 2 alternatively spliced forms of NGN, encoding proteins of 1,461 and 1,408 amino acids. By fluorescence in situ hybridization (FISH) they localized NGN in

15q22, a region infrequently affected by alterations in cancer. NGN transcripts of about 7.5 and 5.5 kb were detected in all adult tissues studied. In contrast to the frequent loss of DCC expression in cancers, no alterations in NGN expression were observed in more than 50 cancers studied, including glioblastoma, medulloblastoma, neuroblastoma, colorectal, breast, cervical, and pancreatic cancer cell lines, and xenografts. Based on their sequence conservation and similar expression during development, Meyerhardt et al. (1997) concluded that DCC and NGN may have related functions; however, the chromosomal location and ubiquitous expression of NGN in various human tumors suggested it is infrequently altered in cancer. Vielmetter et al. (1997) also cloned and characterized human neogenin, and symbolized the gene NEO1. They mapped NEO1 to 15q22.3–q23 by FISH.

[17291] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17292] Meyerhardt, J. A.; Look, A. T.; Bigner, S. H.; Fearon, E. R. : Identification and characterization of neogenin, a DCC-related gene. *Oncogene* 14: 1129–1136, 1997. ; and

[17293] Vielmetter, J.; Kayyem, J. F.; Roman, J. M.; Dreyer, W. J. :

Neogenin, an avian cell surface protein expressed during terminal neuronal differentiation, is closely related to the human.

[17294] Further studies establishing the function and utilities of NEO1 are found in John Hopkins OMIM database record ID 601907, and in cited publications numbered 8889–8891 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Promyelocytic Leukemia (PML, Accession NM_033240) is another VGAM329 host target gene. PML BINDING SITE1 and PML BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by PML, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PML BINDING SITE1 and PML BINDING SITE2, designated SEQ ID:27081 and SEQ ID:27085 respectively, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17295] Another function of VGAM329 is therefore inhibition of Promyelocytic Leukemia (PML, Accession NM_033240). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with PML. Signal Transducer and Activator of Transcription 3 (acute-phase response factor) (STAT3, Accession NM_003150) is another VGAM329 host target gene. STAT3 BINDING SITE1 and STAT3 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by STAT3, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STAT3 BINDING SITE1 and STAT3 BINDING SITE2, designated SEQ ID:9122 and SEQ ID:29269 respectively, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17296] Another function of VGAM329 is therefore inhibition of Signal Transducer and Activator of Transcription 3 (acute-phase response factor) (STAT3, Accession NM_003150), a gene which carries out a dual function: signal transduction and activation of transcription. Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAT3. The function of STAT3 has been established by previous studies. Akira et al. (1994) purified acute-phase response factor (APRF), also designated

STAT3, and cloned the cDNA. At the amino acid level, APRF exhibited 52.5% overall homology with p91, a component of the interferon (IFN)-stimulated gene factor-3 complexes. Also see STAT1 (OMIM Ref. No. 600555).

Caldenhoven et al. (1996) reported the cloning of a cDNA encoding a variant of the transcription factor STAT3, designated STAT3-beta, that was isolated by screening an eosinophil cDNA library. Compared to wildtype STAT3, STAT3-beta lacks an internal domain of 50 bp located near the C terminus. This splice product is a naturally occurring isoform of STAT3 and encodes an 80-kD protein. Animal model experiments lend further support to the function of STAT3. Alternative splicing of the STAT3 gene produces 2 isoforms, STAT3-alpha and a dominant-negative variant, STAT3-beta. In STAT3-beta, the 55 C-terminal residues of STAT3-alpha, spanning the intrinsic transactivation domain, are replaced by 7 distinct residues. Yoo et al. (2002) generated Stat3-beta-deficient mice by gene targeting. Despite intact expression and phosphorylation of Stat3-alpha, overall Stat3 activity was impaired in Stat3-beta -/- cells. Global comparison of transcription in Stat3-beta +/+ and Stat3-beta -/- cells revealed stable differences. Stat3-beta-deficient mice ex-

hibited diminished recovery from endotoxic shock and hyperresponsiveness of a subset of endotoxin-inducible genes in liver. The hepatic response to endotoxin in wild-type mice was accompanied by a transient increase in the ratio of Stat3-beta to Stat3-alpha. These findings indicated a critical role for Stat3-beta in the control of systemic inflammation.

[17297] It is appreciated that the abovementioned animal model for STAT3 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17298] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17299] Caldenhoven, E.; van Dijk, T. B.; Solari, R.; Armstrong, J.; Raaijmakers, J. A. M.; Lammers, J.-W. J.; Koenderman, L.; de Groot, R. P. : STAT3-beta, a splice variant of transcription factor STAT3, is a dominant negative regulator of transcription. J. Biol. Chem. 271: 13221-13227, 1996. ; and

[17300] Yoo, J.-Y.; Huso, D. L.; Nathans, D.; Desiderio, S. : Specific ablation of Stat3-beta distorts the pattern of Stat3-responsive gene expression and impairs recovery

from endotoxic shock.

[17301] Further studies establishing the function and utilities of STAT3 are found in John Hopkins OMIM database record ID 102582, and in cited publications numbered 2339–2343, 3613, 3381, 360 and 9453 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. CCCTC-binding Factor (zinc finger protein)-like (CTCFL, Accession XM_092717) is another VGAM329 host target gene. CTCFL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CTCFL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CTCFL BINDING SITE, designated SEQ ID:40139, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17302] Another function of VGAM329 is therefore inhibition of CCCTC-binding Factor (zinc finger protein)-like (CTCFL, Accession XM_092717). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CTCFL. CYB5-M (Accession XM_170554) is another VGAM329 host target

gene. CYB5-M BINDING SITE1 and CYB5-M BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by CYB5-M, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYB5-M BINDING SITE1 and CYB5-M BINDING SITE2, designated SEQ ID:45378 and SEQ ID:24952 respectively, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17303] Another function of VGAM329 is therefore inhibition of CYB5-M (Accession XM_170554). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYB5-M. Dual Specificity Phosphatase 14 (DUSP14, Accession NM_007026) is another VGAM329 host target gene. DUSP14 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DUSP14, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DUSP14 BINDING SITE, designated SEQ ID:13884, to the nucleotide sequence of VGAM329 RNA,

herein designated VGAM RNA, also designated SEQ ID:3040.

[17304] Another function of VGAM329 is therefore inhibition of Dual Specificity Phosphatase 14 (DUSP14, Accession NM_007026). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DUSP14. Epiregulin (EREG, Accession NM_001432) is another VGAM329 host target gene. EREG BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EREG, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EREG BINDING SITE, designated SEQ ID:7157, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17305] Another function of VGAM329 is therefore inhibition of Epiregulin (EREG, Accession NM_001432). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EREG. FLJ10276 (Accession NM_018045) is another VGAM329 host target gene. FLJ10276 BINDING SITE is HOST TARGET binding site found in the 3' untranslated

region of mRNA encoded by FLJ10276, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10276 BINDING SITE, designated SEQ ID:19793, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17306] Another function of VGAM329 is therefore inhibition of FLJ10276 (Accession NM_018045). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10276. FLJ10315 (Accession NM_018056) is another VGAM329 host target gene. FLJ10315 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ10315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10315 BINDING SITE, designated SEQ ID:19819, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17307] Another function of VGAM329 is therefore inhibition of FLJ10315 (Accession NM_018056). Accordingly, utilities of

VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10315. FLJ10811 (Accession NM_018228) is another VGAM329 host target gene. FLJ10811 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ10811, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10811 BINDING SITE, designated SEQ ID:20166, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17308] Another function of VGAM329 is therefore inhibition of FLJ10811 (Accession NM_018228). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10811. FLJ11336 (Accession NM_018393) is another VGAM329 host target gene. FLJ11336 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ11336, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11336 BINDING SITE,

designated SEQ ID:20431, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17309] Another function of VGAM329 is therefore inhibition of FLJ11336 (Accession NM_018393). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11336. FLJ21865 (Accession NM_022759) is another VGAM329 host target gene. FLJ21865 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21865, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21865 BINDING SITE, designated SEQ ID:23002, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17310] Another function of VGAM329 is therefore inhibition of FLJ21865 (Accession NM_022759). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21865. FLJ23360 (Accession NM_023076) is another VGAM329 host target gene. FLJ23360 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ23360, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23360 BINDING SITE, designated SEQ ID:23335, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17311] Another function of VGAM329 is therefore inhibition of FLJ23360 (Accession NM_023076). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23360. Histidine Triad Nucleotide Binding Protein 3 (HINT3, Accession NM_138571) is another VGAM329 host target gene. HINT3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HINT3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HINT3 BINDING SITE, designated SEQ ID:28879, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17312] Another function of VGAM329 is therefore inhibition of Histidine Triad Nucleotide Binding Protein 3 (HINT3, Accession NM_138571). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HINT3. KIAA0630 (Accession XM_114729) is another VGAM329 host target gene. KIAA0630 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0630, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0630 BINDING SITE, designated SEQ ID:43064, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17313] Another function of VGAM329 is therefore inhibition of KIAA0630 (Accession XM_114729). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0630. KIAA0712 (Accession NM_014715) is another VGAM329 host target gene. KIAA0712 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA0712, corresponding to

a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0712 BINDING SITE, designated SEQ ID:16267, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17314] Another function of VGAM329 is therefore inhibition of KIAA0712 (Accession NM_014715). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0712. KIAA0855 (Accession NM_015003) is another VGAM329 host target gene. KIAA0855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0855 BINDING SITE, designated SEQ ID:17373, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17315] Another function of VGAM329 is therefore inhibition of KIAA0855 (Accession NM_015003). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with KIAA0855. KIAA1001 (Accession NM_014960) is another VGAM329 host target gene. KIAA1001 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1001 BINDING SITE, designated SEQ ID:17329, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17316] Another function of VGAM329 is therefore inhibition of KIAA1001 (Accession NM_014960). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1001. KIAA1018 (Accession NM_014967) is another VGAM329 host target gene. KIAA1018 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1018, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1018 BINDING SITE, designated SEQ ID:17357, to the

nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17317] Another function of VGAM329 is therefore inhibition of KIAA1018 (Accession NM_014967). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1018. KIAA1884 (Accession XM_055539) is another VGAM329 host target gene. KIAA1884 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1884, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1884 BINDING SITE, designated SEQ ID:36298, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17318] Another function of VGAM329 is therefore inhibition of KIAA1884 (Accession XM_055539). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1884. MacGAP (Accession NM_033515) is another VGAM329 host target gene. MacGAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region

of mRNA encoded by MacGAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MacGAP BINDING SITE, designated SEQ ID:27292, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17319] Another function of VGAM329 is therefore inhibition of MacGAP (Accession NM_033515). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MacGAP. Phosphatidylinositol-4-phosphate 5-kinase, Type I, Gamma (PIP5K1C, Accession XM_047620) is another VGAM329 host target gene. PIP5K1C BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PIP5K1C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PIP5K1C BINDING SITE, designated SEQ ID:35018, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17320] Another function of VGAM329 is therefore inhibition of

Phosphatidylinositol-4-phosphate 5-kinase, Type I, Gamma (PIP5K1C, Accession XM_047620). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PIP5K1C. PRO1855 (Accession NM_018509) is another VGAM329 host target gene. PRO1855 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PRO1855, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO1855 BINDING SITE, designated SEQ ID:20577, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17321] Another function of VGAM329 is therefore inhibition of PRO1855 (Accession NM_018509). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO1855. RPH3A (Accession NM_014954) is another VGAM329 host target gene. RPH3A BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RPH3A, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of RPH3A BINDING SITE, designated SEQ ID:17309, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17322] Another function of VGAM329 is therefore inhibition of RPH3A (Accession NM_014954). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RPH3A. T-box 19 (TBX19, Accession NM_005149) is another VGAM329 host target gene. TBX19 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TBX19, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TBX19 BINDING SITE, designated SEQ ID:11625, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17323] Another function of VGAM329 is therefore inhibition of T-box 19 (TBX19, Accession NM_005149). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

TBX19. Tripartite Motif-containing 4 (TRIM4, Accession NM_033017) is another VGAM329 host target gene. TRIM4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TRIM4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TRIM4 BINDING SITE, designated SEQ ID:26905, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17324] Another function of VGAM329 is therefore inhibition of Tripartite Motif-containing 4 (TRIM4, Accession NM_033017). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TRIM4. LOC116228 (Accession XM_057659) is another VGAM329 host target gene. LOC116228 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC116228, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC116228 BINDING SITE, designated SEQ ID:36536, to the nucleotide sequence of

VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17325] Another function of VGAM329 is therefore inhibition of LOC116228 (Accession XM_057659). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC116228. LOC134145 (Accession XM_059691) is another VGAM329 host target gene. LOC134145 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC134145, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC134145 BINDING SITE, designated SEQ ID:37061, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17326] Another function of VGAM329 is therefore inhibition of LOC134145 (Accession XM_059691). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC134145. LOC145980 (Accession XM_096914) is another VGAM329 host target gene. LOC145980 BINDING SITE is HOST TARGET binding site found in the 5' un-

translated region of mRNA encoded by LOC145980, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145980 BINDING SITE, designated SEQ ID:40649, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17327] Another function of VGAM329 is therefore inhibition of LOC145980 (Accession XM_096914). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145980. LOC145988 (Accession XM_085290) is another VGAM329 host target gene. LOC145988 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145988, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145988 BINDING SITE, designated SEQ ID:38037, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17328] Another function of VGAM329 is therefore inhibition of LOC145988 (Accession XM_085290). Accordingly, utilities

of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145988. LOC146901 (Accession XM_097121) is another VGAM329 host target gene. LOC146901 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146901, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146901 BINDING SITE, designated SEQ ID:40763, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17329] Another function of VGAM329 is therefore inhibition of LOC146901 (Accession XM_097121). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146901. LOC150166 (Accession XM_097824) is another VGAM329 host target gene. LOC150166 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150166, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences

of LOC150166 BINDING SITE, designated SEQ ID:41147, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17330] Another function of VGAM329 is therefore inhibition of LOC150166 (Accession XM_097824). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150166. LOC151429 (Accession XM_098059) is another VGAM329 host target gene. LOC151429 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC151429, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC151429 BINDING SITE, designated SEQ ID:41345, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17331] Another function of VGAM329 is therefore inhibition of LOC151429 (Accession XM_098059). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC151429. LOC162333 (Accession XM_102591) is another VGAM329 host target gene. LOC162333 BINDING

SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC162333, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC162333 BINDING SITE, designated SEQ ID:42142, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17332] Another function of VGAM329 is therefore inhibition of LOC162333 (Accession XM_102591). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC162333. LOC199920 (Accession XM_114056) is another VGAM329 host target gene. LOC199920 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC199920, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC199920 BINDING SITE, designated SEQ ID:42660, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17333] Another function of VGAM329 is therefore inhibition of

LOC199920 (Accession XM_114056). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC199920. LOC200734 (Accession XM_114286) is another VGAM329 host target gene. LOC200734 BINDING SITE1 and LOC200734 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by LOC200734, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200734 BINDING SITE1 and LOC200734 BINDING SITE2, designated SEQ ID:42843 and SEQ ID:42844 respectively, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17334] Another function of VGAM329 is therefore inhibition of LOC200734 (Accession XM_114286). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200734. LOC51337 (Accession NM_016647) is another VGAM329 host target gene. LOC51337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51337, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51337 BINDING SITE, designated SEQ ID:18764, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17335] Another function of VGAM329 is therefore inhibition of LOC51337 (Accession NM_016647). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51337. LOC83690 (Accession NM_031461) is another VGAM329 host target gene. LOC83690 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC83690, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC83690 BINDING SITE, designated SEQ ID:25486, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17336] Another function of VGAM329 is therefore inhibition of LOC83690 (Accession NM_031461). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC83690. LOC90917 (Accession XM_034861) is another VGAM329 host target gene. LOC90917 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by LOC90917, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC90917 BINDING SITE, designated SEQ ID:32171, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17337] Another function of VGAM329 is therefore inhibition of LOC90917 (Accession XM_034861). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC90917. LOC91149 (Accession XM_036480) is another VGAM329 host target gene. LOC91149 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by LOC91149, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC91149 BINDING SITE, designated SEQ ID:32460, to the

nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17338] Another function of VGAM329 is therefore inhibition of LOC91149 (Accession XM_036480). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC91149. LOC92568 (Accession XM_045852) is another VGAM329 host target gene. LOC92568 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92568, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92568 BINDING SITE, designated SEQ ID:34581, to the nucleotide sequence of VGAM329 RNA, herein designated VGAM RNA, also designated SEQ ID:3040.

[17339] Another function of VGAM329 is therefore inhibition of LOC92568 (Accession XM_045852). Accordingly, utilities of VGAM329 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92568. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 330 (VGAM330) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17340] VGAM330 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM330 was detected is described hereinabove with reference to Figs. 1–8.

[17341] VGAM330 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17342] VGAM330 gene encodes a VGAM330 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM330

precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM330 precursor RNA is designated SEQ ID:316, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:316 is located at position 43800 relative to the genome of Human Herpesvirus 5.

[17343] VGAM330 precursor RNA folds onto itself, forming VGAM330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17344] An enzyme complex designated DICER COMPLEX, `dices` the VGAM330 folded precursor RNA into VGAM330 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other

necessary proteins. A probable (over 76%) nucleotide sequence of VGAM330 RNA is designated SEQ ID:3041, and is provided hereinbelow with reference to the sequence listing part.

[17345] VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM330 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5' untranslated region, a protein coding region and a 3' untranslated region, designated 5'UTR, PROTEIN CODING and 3'UTR respectively.

[17346] VGAM330 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM330 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the

number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM330 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17347] The complementary binding of VGAM330 RNA, herein designated VGAM RNA, to host target binding sites on VGAM330 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM330 host target RNA into VGAM330 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17348] It is appreciated that VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM330 host target genes. The mRNA of each one of this plurality of VGAM330 host target genes

comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM330 RNA, herein designated VGAM RNA, and which when bound by VGAM330 RNA causes inhibition of translation of respective one or more VGAM330 host target proteins.

[17349] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM330 gene, herein designated VGAM GENE, on one or more VGAM330 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17350] It is yet further appreciated that a function of VGAM330 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM330 correlate with, and may be deduced from, the identity of the host target genes which VGAM330 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17351] Nucleotide sequences of the VGAM330 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM330 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM330 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM330 are further described hereinbelow with reference to Table 1.

[17352] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM330 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM330 RNA, herein designated VGAM RNA, are described hereinbelow with refer-

ence to Table 2.

[17353] As mentioned hereinabove with reference to Fig. 1, a function of VGAM330 gene, herein designated VGAM is inhibition of expression of VGAM330 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM330 correlate with, and may be deduced from, the identity of the target genes which VGAM330 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17354] Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM_053056) is a VGAM330 host target gene. CCND1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CCND1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CCND1 BINDING SITE, designated SEQ ID:27600, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17355] A function of VGAM330 is therefore inhibition of Cyclin D1 (PRAD1: parathyroid adenomatosis 1) (CCND1, Accession NM_053056), a gene which is involved in the control

of cell cycle and is required for Schwann cell proliferation to proceed normally during Wallerian degeneration. Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CCND1. The function of CCND1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM220. Centromere Protein A, 17kDa (CENPA, Accession NM_001809) is another VGAM330 host target gene. CENPA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CENPA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CENPA BINDING SITE, designated SEQ ID:7559, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17356] Another function of VGAM330 is therefore inhibition of Centromere Protein A, 17kDa (CENPA, Accession NM_001809), a gene which is a component of a modified nucleosome or nucleosome-like structure . Accordingly, utilities of VGAM330 include diagnosis, prevention and

treatment of diseases and clinical conditions associated with CENPA. The function of CENPA has been established by previous studies. CENPA is a 17-kD centromere protein that was identified along with CENPB and CENPC (OMIM Ref. No. 117141) using centromere-specific autoantibodies from CREST (see OMIM Ref. No. 181750) patients. Palmer et al. (1991) purified CENPA protein from bull sperm nuclei and obtained a partial amino acid sequence. They found that some CENPA sequences are highly similar to regions of histone H3. Sullivan et al. (1994) cloned a bovine CENPA cDNA by RT-PCR using primers based on the bovine CENPA protein sequence. By screening a human endothelial cell cDNA library with the bovine cDNA, they isolated a human CENPA cDNA. The C-terminal region of the predicted 140-amino acid human protein shares 62% amino acid identity with that of histone H3.1. Epitope-tagged CENPA protein colocalized with centromeres when expressed in HeLa cells. The centromere-targeting signals of CENPA are located within the histone H3-homologous region. Sullivan et al. (1994) suggested that CENPA is a component of a modified nucleosome or nucleosome-like structure in which it replaces 1 or both copies of conventional histone H3 in the (H3-H4)₂

tetrameric core of the nucleosome particle. Animal model experiments lend further support to the function of CENPA. Using gene targeting, Howman et al. (2000) disrupted the mouse Cenpa gene and demonstrated that the gene is essential. Heterozygous mice were healthy and fertile, whereas null mutants failed to survive beyond 6.5 days postconception. Affected embryos showed severe mitotic problems, including micronuclei and macronuclei formation, nuclear bridging and blebbing, and chromatin fragmentation and hypercondensation. Immunofluorescence analysis of cells at day 5.5 revealed complete Cenpa depletion, diffuse Cenpb foci, absence of discrete Cenpc signal on centromeres, and dispersion of Cenpb and Cenpc throughout the nucleus. These results suggested that Cenpa is essential for kinetochore targeting of Cenpc and plays an early role in organizing centromeric chromatin at interphase. The evidence was consistent with the proposal of a critical epigenetic function for CENPA in marking a chromosomal region for centromere formation.

[17357] It is appreciated that the abovementioned animal model for CENPA is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications sited hereinbelow.

[17358] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17359] Palmer, D. K.; O'Day, K.; Trong, H. L.; Charbonneau, H.; Margolis, R. L. : Purification of the centromere-specific protein CENP-A and demonstration that it is a distinctive histone. *Proc. Nat. Acad. Sci.* 88: 3734-3738, 1991. ; and

[17360] Sullivan, K. F.; Hechenberger, M.; Masri, K. : Human CENP-A contains a histone H3 related histone fold domain that is required for targeting to the centromere. *J. Cell Biol.* 127: 581-59.

[17361] Further studies establishing the function and utilities of CENPA are found in John Hopkins OMIM database record ID 117139, and in cited publications numbered 4666-4670 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Dihydropyrimidine Dehydrogenase (DPYD, Accession XM_017469) is another VGAM330 host target gene. DPYD BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DPYD, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

DPYD BINDING SITE, designated SEQ ID:30316, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17362] Another function of VGAM330 is therefore inhibition of Dihydropyrimidine Dehydrogenase (DPYD, Accession XM_017469). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DPYD. EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883) is another VGAM330 host target gene. EGFL4 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by EGFL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of EGFL4 BINDING SITE, designated SEQ ID:30968, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17363] Another function of VGAM330 is therefore inhibition of EGF-like-domain, Multiple 4 (EGFL4, Accession XM_029883). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EGFL4. Homeo Box D4

(HOXD4, Accession NM_014621) is another VGAM330 host target gene. HOXD4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HOXD4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HOXD4 BINDING SITE, designated SEQ ID:15977, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17364] Another function of VGAM330 is therefore inhibition of Homeo Box D4 (HOXD4, Accession NM_014621), a gene which is part of a developmental regulatory system. Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HOXD4. The function of HOXD4 has been established by previous studies. See HOXD3 (OMIM Ref. No. 142980). The homologous mouse gene was at first designated a Hox-5 gene. HOX4 genes, other than the one subsequently designated HOX4A, were initially considered to be members of a different cluster of genes called HOX5. Oliver et al. (1989) found by study of interspecific somatic cell hybrids that the cluster of so-called

HOX5 genes map to human chromosome 2. By in situ hybridization, they found that the localization was 2q31–q32 with a peak of grains at 2q32.3. This gene is also called HOXD4, as a member of the HOXD gene cluster on 2q31. Mavilio et al. (1986) described the HOXD4 gene, but designated it homeo box X. Northern blot analysis detected multiple embryonic transcripts, which were differentially expressed in spinal cord, brain, backbone rudiments, limb buds, and heart in 5- to 9-week-old human embryos and fetuses in a striking organ- and stage-specific pattern. On the basis of these observations, Mavilio et al. (1986) suggested that in early mammalian development, homeo box genes may exert a wide spectrum of control functions in a variety of organs and body parts in addition to the spinal cord.

[17365] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17366] Mavilio, F.; Simeone, A.; Giampaolo, A.; Faiella, A.; Zapavigna, V.; Acampora, D.; Poiana, G.; Russo, G.; Peschle, C.; Boncinelli, E. : Differential and stage-related expression in embryonic tissues of a new human homoeobox gene. Nature 324: 664–668, 1986. ; and

[17367] Oliver, G.; Sidell, N.; Fiske, W.; Heinzmann, C.; Mohandas, T.; Sparkes, R. S.; De Robertis, E. M. : Complementary homeo protein gradients in developing limb buds. *Genes Dev.* 3: 641–650.

[17368] Further studies establishing the function and utilities of HOXD4 are found in John Hopkins OMIM database record ID 142981, and in cited publications numbered 3188–318 and 3187 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. WD Repeat Domain 1 (WDR1, Accession NM_017491) is another VGAM330 host target gene. WDR1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by WDR1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WDR1 BINDING SITE, designated SEQ ID:18954, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17369] Another function of VGAM330 is therefore inhibition of WD Repeat Domain 1 (WDR1, Accession NM_017491). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions as–

sociated with WDR1. AFAP (Accession NM_021638) is another VGAM330 host target gene. AFAP BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by AFAP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AFAP BINDING SITE, designated SEQ ID:22290, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17370] Another function of VGAM330 is therefore inhibition of AFAP (Accession NM_021638). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AFAP. Rho Guanine Nucleotide Exchange Factor (GEF) 15 (ARHGEF15, Accession NM_014958) is another VGAM330 host target gene. ARHGEF15 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ARHGEF15, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ARHGEF15 BINDING SITE, designated SEQ ID:17315, to the nucleotide sequence of

VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17371] Another function of VGAM330 is therefore inhibition of Rho Guanine Nucleotide Exchange Factor (GEF) 15 (ARHGEF15, Accession NM_014958). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ARHGEF15. Activating Transcription Factor 3 (ATF3, Accession NM_004024) is another VGAM330 host target gene. ATF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATF3 BINDING SITE, designated SEQ ID:10241, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17372] Another function of VGAM330 is therefore inhibition of Activating Transcription Factor 3 (ATF3, Accession NM_004024). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATF3. FLJ12409 (Accession NM_025105) is another VGAM330 host target gene.

FLJ12409 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12409, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12409 BINDING SITE, designated SEQ ID:24752, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17373] Another function of VGAM330 is therefore inhibition of FLJ12409 (Accession NM_025105). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12409. FLJ12783 (Accession NM_031426) is another VGAM330 host target gene. FLJ12783 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12783, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12783 BINDING SITE, designated SEQ ID:25420, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17374] Another function of VGAM330 is therefore inhibition of FLJ12783 (Accession NM_031426). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12783. FLJ12910 (Accession NM_024573) is another VGAM330 host target gene. FLJ12910 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by FLJ12910, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12910 BINDING SITE, designated SEQ ID:23800, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17375] Another function of VGAM330 is therefore inhibition of FLJ12910 (Accession NM_024573). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12910. FLJ14251 (Accession NM_024881) is another VGAM330 host target gene. FLJ14251 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14251, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14251 BINDING SITE, designated SEQ ID:24325, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17376] Another function of VGAM330 is therefore inhibition of FLJ14251 (Accession NM_024881). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14251. FLJ20315 (Accession NM_017763) is another VGAM330 host target gene. FLJ20315 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by FLJ20315, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20315 BINDING SITE, designated SEQ ID:19380, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17377] Another function of VGAM330 is therefore inhibition of FLJ20315 (Accession NM_017763). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20315.

FLJ21162 (Accession NM_024873) is another VGAM330 host target gene. FLJ21162 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ21162, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ21162 BINDING SITE, designated SEQ ID:24307, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17378] Another function of VGAM330 is therefore inhibition of FLJ21162 (Accession NM_024873). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ21162. FLJ23342 (Accession NM_024631) is another VGAM330 host target gene. FLJ23342 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ23342, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ23342 BINDING SITE, designated SEQ ID:23898, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also desig-

nated SEQ ID:3041.

[17379] Another function of VGAM330 is therefore inhibition of FLJ23342 (Accession NM_024631). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ23342. HH114 (Accession NM_032499) is another VGAM330 host target gene. HH114 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HH114, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HH114 BINDING SITE, designated SEQ ID:26251, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17380] Another function of VGAM330 is therefore inhibition of HH114 (Accession NM_032499). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HH114. KIAA0798 (Accession NM_014650) is another VGAM330 host target gene. KIAA0798 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0798, corresponding to a HOST TARGET

binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0798 BINDING SITE, designated SEQ ID:16072, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17381] Another function of VGAM330 is therefore inhibition of KIAA0798 (Accession NM_014650). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0798. Mannosidase, Beta A, Lysosomal-like (MANBAL, Accession NM_022077) is another VGAM330 host target gene. MANBAL BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MANBAL, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MANBAL BINDING SITE, designated SEQ ID:22621, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17382] Another function of VGAM330 is therefore inhibition of Mannosidase, Beta A, Lysosomal-like (MANBAL, Accession

NM_022077). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MANBAL. Opiate Receptor-like 1 (OPRL1, Accession NM_000913) is another VGAM330 host target gene. OPRL1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by OPRL1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of OPRL1 BINDING SITE, designated SEQ ID:6616, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17383] Another function of VGAM330 is therefore inhibition of Opiate Receptor-like 1 (OPRL1, Accession NM_000913). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with OPRL1. Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 6 (SLC17A6, Accession NM_020346) is another VGAM330 host target gene. SLC17A6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC17A6, corresponding to a

HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC17A6 BINDING SITE, designated SEQ ID:21595, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17384] Another function of VGAM330 is therefore inhibition of Solute Carrier Family 17 (sodium-dependent inorganic phosphate cotransporter), Member 6 (SLC17A6, Accession NM_020346). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC17A6. LOC139221 (Accession XM_066558) is another VGAM330 host target gene. LOC139221 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139221, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139221 BINDING SITE, designated SEQ ID:37331, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17385] Another function of VGAM330 is therefore inhibition of

LOC139221 (Accession XM_066558). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139221. LOC145844 (Accession XM_085255) is another VGAM330 host target gene. LOC145844 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC145844, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145844 BINDING SITE, designated SEQ ID:37999, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17386] Another function of VGAM330 is therefore inhibition of LOC145844 (Accession XM_085255). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145844. LOC150290 (Accession XM_086863) is another VGAM330 host target gene. LOC150290 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC150290, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC150290 BINDING SITE, designated SEQ ID:38933, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17387] Another function of VGAM330 is therefore inhibition of LOC150290 (Accession XM_086863). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC150290. LOC164382 (Accession XM_104390) is another VGAM330 host target gene. LOC164382 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC164382, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC164382 BINDING SITE, designated SEQ ID:42161, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17388] Another function of VGAM330 is therefore inhibition of LOC164382 (Accession XM_104390). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC164382. LOC203350 (Accession XM_117536) is an-

other VGAM330 host target gene. LOC203350 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC203350, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC203350 BINDING SITE, designated SEQ ID:43528, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17389] Another function of VGAM330 is therefore inhibition of LOC203350 (Accession XM_117536). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC203350. LOC221362 (Accession XM_168093) is another VGAM330 host target gene. LOC221362 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221362, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221362 BINDING SITE, designated SEQ ID:45021, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17390] Another function of VGAM330 is therefore inhibition of LOC221362 (Accession XM_168093). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221362. LOC222060 (Accession XM_168427) is another VGAM330 host target gene. LOC222060 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC222060, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC222060 BINDING SITE, designated SEQ ID:45157, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17391] Another function of VGAM330 is therefore inhibition of LOC222060 (Accession XM_168427). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC222060. LOC254413 (Accession XM_173141) is another VGAM330 host target gene. LOC254413 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC254413, corresponding to a HOST TARGET binding site such as BIND-

ING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254413 BINDING SITE, designated SEQ ID:46396, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17392] Another function of VGAM330 is therefore inhibition of LOC254413 (Accession XM_173141). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254413. LOC92573 (Accession XM_045884) is another VGAM330 host target gene. LOC92573 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC92573, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92573 BINDING SITE, designated SEQ ID:34601, to the nucleotide sequence of VGAM330 RNA, herein designated VGAM RNA, also designated SEQ ID:3041.

[17393] Another function of VGAM330 is therefore inhibition of LOC92573 (Accession XM_045884). Accordingly, utilities of VGAM330 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC92573. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 331 (VGAM331) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17394] VGAM331 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM331 was detected is described hereinabove with reference to Figs. 1–8.

[17395] VGAM331 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 5. VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17396] VGAM331 gene encodes a VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM331 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM331 precursor RNA is designated SEQ ID:317, and is provided hereinbelow with reference to the

sequence listing part. Nucleotide sequence SEQ ID:317 is located at position 113291 relative to the genome of Human Herpesvirus 5.

[17397] VGAM331 precursor RNA folds onto itself, forming VGAM331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17398] An enzyme complex designated DICER COMPLEX, `dices` the VGAM331 folded precursor RNA into VGAM331 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 70%) nucleotide sequence of VGAM331 RNA is designated SEQ ID:3042, and is provided hereinbelow with reference to the sequence listing part.

[17399] VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM331 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17400] VGAM331 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM331 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM331 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in

untranslated regions of a VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17401] The complementary binding of VGAM331 RNA, herein designated VGAM RNA, to host target binding sites on VGAM331 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM331 host target RNA into VGAM331 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17402] It is appreciated that VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM331 host target genes. The mRNA of each one of this plurality of VGAM331 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM331 RNA, herein designated VGAM RNA, and which when bound by VGAM331 RNA causes in-

hibition of translation of respective one or more VGAM331 host target proteins.

[17403] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM331 gene, herein designated VGAM GENE, on one or more VGAM331 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17404] It is yet further appreciated that a function of VGAM331 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM331 include diagnosis, prevention and

treatment of viral infection by Human Herpesvirus 5. Specific functions, and accordingly utilities, of VGAM331 correlate with, and may be deduced from, the identity of the host target genes which VGAM331 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17405] Nucleotide sequences of the VGAM331 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM331 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM331 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM331 are further described hereinbelow with reference to Table 1.

[17406] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM331 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM331 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17407] As mentioned hereinabove with reference to Fig. 1, a function of VGAM331 gene, herein designated VGAM is inhibition of expression of VGAM331 target genes. It is

appreciated that specific functions, and accordingly utilities, of VGAM331 correlate with, and may be deduced from, the identity of the target genes which VGAM331 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17408] BTB and CNC Homology 1, Basic Leucine Zipper Transcription Factor 2 (BACH2, Accession NM_021813) is a VGAM331 host target gene. BACH2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BACH2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BACH2 BINDING SITE, designated SEQ ID:22381, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17409] A function of VGAM331 is therefore inhibition of BTB and CNC Homology 1, Basic Leucine Zipper Transcription Factor 2 (BACH2, Accession NM_021813), a gene which acts as repressor or activator, binds to maf recognition elements. Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BACH2. The function of BACH2 has

been established by previous studies. By screening a K562 erythroleukemia cell line with mouse Bach2 cDNA as the probe, Sasaki et al. (2000) isolated a cDNA encoding BACH2. The deduced 841-amino acid protein is 89.5% identical to mouse Bach2, with 97% identity shared in the BTB and bZip functional domains and 94% identity shared in the serine-rich region. Northern blot analysis revealed expression of an approximately 11.0-kb BACH2 transcript restricted to thymus, spleen, and leukocytes; low levels were also detected in small intestine and brain. Sasaki et al. (2000) found mRNA and protein expression primarily in B-lymphoid rather than other hematopoietic cell lines. RT-PCR analysis showed that BACH2, like mouse Bach2, is expressed in primary B cells at the progenitor, precursor, immature, and mature B-cell stages. Mouse Bach2 is not expressed in plasma cells (Muto et al., 1998). Gel shift analysis showed that when overexpressed, BACH2 binds to MAF recognition elements (MARE). Overexpression also resulted in a loss of clonogenic activity. Southern blot analysis determined that BACH2 is a single-copy gene. BACH2/CA-1 microsatellite analysis indicated that loss of heterozygosity occurred in 5 of 25 non-Hodgkin lymphoma (OMIM Ref. No. 605027) patients.

[17410] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17411] Sasaki, S.; Ito, E.; Toki, T.; Maekawa, T.; Kanezaki, R.; Umenai, T.; Muto, A.; Nagai, H.; Kinoshita, T.; Yamamoto, M.; Inazawa, J.; Taketo, M. M.; Nakahata, T.; Igarashi, K.; Yokoyama, M. : Cloning and expression of human B cell-specific transcription factor BACH2 mapped to chromosome 6q15. *Oncogene* 19: 3739–3749, 2000. ; and

[17412] Muto, A.; Hoshino, H.; Madisen, L.; Yanai, N.; Obinata, M.; Karasuyama, H.; Hayashi, N.; Nakauchi, H.; Yamamoto, M.; Groudine, M.; Igarashi, K. : Identification of Bach2 as a B-cell-spe.

[17413] Further studies establishing the function and utilities of BACH2 are found in John Hopkins OMIM database record ID 605394, and in cited publications numbered 731 and 7312 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_032982) is another VGAM331 host target gene. CASP2 BINDING SITE1 through CASP2 BINDING SITE4 are HOST TARGET binding sites found in untranslated re-

gions of mRNA encoded by CASP2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CASP2 BINDING SITE1 through CASP2 BINDING SITE4, designated SEQ ID:26855, SEQ ID:26860, SEQ ID:26865 and SEQ ID:6892 respectively, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17414] Another function of VGAM331 is therefore inhibition of Caspase 2, Apoptosis-related Cysteine Protease (neural precursor cell expressed, developmentally down-regulated 2) (CASP2, Accession NM_032982), a gene which involves in the activation cascade of caspases responsible for apoptosis execution. Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CASP2. The function of CASP2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM148.H3 Histone, Family 3B (H3.3B) (H3F3B, Accession NM_005324) is another VGAM331 host target gene. H3F3B BINDING SITE is HOST TARGET binding site found

in the 3' untranslated region of mRNA encoded by H3F3B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of H3F3B BINDING SITE, designated SEQ ID:11797, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17415] Another function of VGAM331 is therefore inhibition of H3 Histone, Family 3B (H3.3B) (H3F3B, Accession NM_005324). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with H3F3B. Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876) is another VGAM331 host target gene. IGF2R BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by IGF2R, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of IGF2R BINDING SITE, designated SEQ ID:6559, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17416] Another function of VGAM331 is therefore inhibition of Insulin-like Growth Factor 2 Receptor (IGF2R, Accession NM_000876), a gene which transport of phosphorylated lysosomal enzymes from the golgi complex and the cell surface to lysosomes. lysosomal enzymes bearing phosphomannosyl residues bind specifically to mannose-6-phosphate receptors in the golgi apparatus and the resulting receptor-ligand complex is transported to an acidic prelysosomal compartment where the low pH mediates the dissociation of the complex. this receptor also binds insulin growth factor ii. Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with IGF2R. The function of IGF2R and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM209. Src Homology Three (SH3) and Cysteine Rich Domain (STAC, Accession NM_003149) is another VGAM331 host target gene. STAC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by STAC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complemen-

tarity of the nucleotide sequences of STAC BINDING SITE, designated SEQ ID:9121, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17417] Another function of VGAM331 is therefore inhibition of Src Homology Three (SH3) and Cysteine Rich Domain (STAC, Accession NM_003149), a gene which is probably involved in a neuron-specific signal transduction. Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STAC. The function of STAC has been established by previous studies. RLGS-M (restriction landmark genomic scanning using methylation-sensitive endonuclease) is a method for scanning the methylation status of large sections of a genome. Using RLGS-M to scan mouse brain genomic DNA from various developmental stages, Suzuki et al. (1996) found a tissue-specific gel spot whose intensity changed developmentally. The gene corresponding to this spot, which they termed Stac (for Src homology 3 and cysteine-rich domains), encodes a predicted 403-amino acid protein. The mouse Stac gene was used to clone human STAC from a fetal brain cDNA library. The predicted 402-amino acid STAC protein is 83% identical to

that of mouse. Suzuki et al. (1996) noted that cysteine-rich and SH3 domains are frequently found in signal transduction proteins, and suggested that STAC may play a role in the neuron-specific signal transduction pathway. Kawai et al. (1998) mapped the human STAC gene to 3p24-p22 using PCR of a radiation hybrid panel. The mouse Stac gene was mapped by interspecific backcross analysis to the distal portion of chromosome 9, in a region syntenic with human chromosome 3p21.

[17418] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17419] Kawai, J.; Suzuki, H.; Hara, A.; Hirose, K.; Watanabe, S. : Human and mouse chromosomal mapping of Stac, a neuron-specific protein with an SH3 domain. Genomics 47: 140-142, 1998. ; and

[17420] Suzuki, H.; Kawai, J.; Taga, C.; Yaoi, T.; Hara, A.; Hirose, K.; Hayashizaki, Y.; Watanabe, S. : Stac, a novel neuron-specific protein with cysteine-rich and SH3 domains. Biochem. Bioph.

[17421] Further studies establishing the function and utilities of STAC are found in John Hopkins OMIM database record ID 602317, and in cited publications numbered 6297-6298

listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Zinc Finger Protein 264 (ZNF264, Accession NM_003417) is another VGAM331 host target gene. ZNF264 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ZNF264, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ZNF264 BINDING SITE, designated SEQ ID:9462, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17422] Another function of VGAM331 is therefore inhibition of Zinc Finger Protein 264 (ZNF264, Accession NM_003417). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ZNF264. Butyrophilin, Subfamily 3, Member A1 (BTN3A1, Accession NM_007048) is another VGAM331 host target gene. BTN3A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BTN3A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BTN3A1 BINDING SITE, designated SEQ ID:9463, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3043.

tarity of the nucleotide sequences of BTN3A1 BINDING SITE, designated SEQ ID:13922, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17423] Another function of VGAM331 is therefore inhibition of Butyrophilin, Subfamily 3, Member A1 (BTN3A1, Accession NM_007048). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BTN3A1. Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456) is another VGAM331 host target gene. C13orf1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C13orf1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C13orf1 BINDING SITE, designated SEQ ID:21694, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17424] Another function of VGAM331 is therefore inhibition of Chromosome 13 Open Reading Frame 1 (C13orf1, Accession NM_020456). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and

clinical conditions associated with C13orf1. Cyclin M1 (CNNM1, Accession NM_020348) is another VGAM331 host target gene. CNNM1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CNNM1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CNNM1 BINDING SITE, designated SEQ ID:21613, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17425] Another function of VGAM331 is therefore inhibition of Cyclin M1 (CNNM1, Accession NM_020348). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CNNM1. FLJ12960 (Accession NM_024638) is another VGAM331 host target gene. FLJ12960 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12960, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12960 BINDING SITE, designated SEQ ID:23920, to the nucleotide

sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17426] Another function of VGAM331 is therefore inhibition of FLJ12960 (Accession NM_024638). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12960. FLJ20813 (Accession NM_017961) is another VGAM331 host target gene. FLJ20813 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20813, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20813 BINDING SITE, designated SEQ ID:19679, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17427] Another function of VGAM331 is therefore inhibition of FLJ20813 (Accession NM_017961). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20813. FLJ31101 (Accession NM_017964) is another VGAM331 host target gene. FLJ31101 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA

encoded by FLJ31101, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ31101 BINDING SITE, designated SEQ ID:19686, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17428] Another function of VGAM331 is therefore inhibition of FLJ31101 (Accession NM_017964). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ31101. General Transcription Factor IIE, Polypeptide 1, Alpha 56kDa (GTF2E1, Accession NM_005513) is another VGAM331 host target gene. GTF2E1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GTF2E1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GTF2E1 BINDING SITE, designated SEQ ID:12037, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17429] Another function of VGAM331 is therefore inhibition of

General Transcription Factor IIE, Polypeptide 1, Alpha 56kDa (GTF2E1, Accession NM_005513). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GTF2E1. HSPC065 (Accession NM_014157) is another VGAM331 host target gene. HSPC065 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by HSPC065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15455, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17430] Another function of VGAM331 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. KIAA0450 (Accession NM_014638) is another VGAM331 host target gene. KIAA0450 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by KIAA0450, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or

BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0450 BINDING SITE, designated SEQ ID:16037, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17431] Another function of VGAM331 is therefore inhibition of KIAA0450 (Accession NM_014638). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0450. KIAA1143 (Accession XM_044014) is another VGAM331 host target gene. KIAA1143 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1143, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1143 BINDING SITE, designated SEQ ID:34077, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17432] Another function of VGAM331 is therefore inhibition of KIAA1143 (Accession XM_044014). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1143. PRO0365 (Accession NM_014126) is another VGAM331 host target gene. PRO0365 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by PRO0365, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRO0365 BINDING SITE, designated SEQ ID:15390, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17433] Another function of VGAM331 is therefore inhibition of PRO0365 (Accession NM_014126). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRO0365. RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM_031296) is another VGAM331 host target gene. RAB33B BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB33B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB33B BINDING SITE, designated SEQ ID:25332, to the nucleotide sequence of VGAM331 RNA,

herein designated VGAM RNA, also designated SEQ ID:3042.

[17434] Another function of VGAM331 is therefore inhibition of RAB33B, Member RAS Oncogene Family (RAB33B, Accession NM_031296). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB33B. TUCAN (Accession NM_014959) is another VGAM331 host target gene. TUCAN BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by TUCAN, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUCAN BINDING SITE, designated SEQ ID:17319, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17435] Another function of VGAM331 is therefore inhibition of TUCAN (Accession NM_014959). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUCAN. LOC130535 (Accession XM_072244) is another VGAM331 host target gene. LOC130535 BINDING SITE is HOST TAR-

GET binding site found in the 3' untranslated region of mRNA encoded by LOC130535, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC130535 BINDING SITE, designated SEQ ID:37478, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17436] Another function of VGAM331 is therefore inhibition of LOC130535 (Accession XM_072244). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC130535. LOC143879 (Accession XM_084666) is another VGAM331 host target gene. LOC143879 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC143879, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC143879 BINDING SITE, designated SEQ ID:37660, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17437] Another function of VGAM331 is therefore inhibition of

LOC143879 (Accession XM_084666). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC143879. LOC146854 (Accession XM_085618) is another VGAM331 host target gene. LOC146854 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC146854, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146854 BINDING SITE, designated SEQ ID:38255, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17438] Another function of VGAM331 is therefore inhibition of LOC146854 (Accession XM_085618). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146854. LOC146909 (Accession XM_085634) is another VGAM331 host target gene. LOC146909 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146909, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 il-

illustrates the complementarity of the nucleotide sequences of LOC146909 BINDING SITE, designated SEQ ID:38269, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17439] Another function of VGAM331 is therefore inhibition of LOC146909 (Accession XM_085634). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146909. LOC169693 (Accession XM_108998) is another VGAM331 host target gene. LOC169693 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC169693, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC169693 BINDING SITE, designated SEQ ID:42208, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17440] Another function of VGAM331 is therefore inhibition of LOC169693 (Accession XM_108998). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC169693. LOC200014 (Accession XM_114087) is an-

other VGAM331 host target gene. LOC200014 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC200014, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200014 BINDING SITE, designated SEQ ID:42694, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17441] Another function of VGAM331 is therefore inhibition of LOC200014 (Accession XM_114087). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200014. LOC55893 (Accession NM_018660) is another VGAM331 host target gene. LOC55893 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC55893, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC55893 BINDING SITE, designated SEQ ID:20731, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17442] Another function of VGAM331 is therefore inhibition of LOC55893 (Accession NM_018660). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC55893. LOC89919 (Accession XM_027244) is another VGAM331 host target gene. LOC89919 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC89919, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC89919 BINDING SITE, designated SEQ ID:30465, to the nucleotide sequence of VGAM331 RNA, herein designated VGAM RNA, also designated SEQ ID:3042.

[17443] Another function of VGAM331 is therefore inhibition of LOC89919 (Accession XM_027244). Accordingly, utilities of VGAM331 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC89919. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 332 (VGAM332) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[17444] VGAM332 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM332 was detected is described hereinabove with reference to Figs. 1–8.

[17445] VGAM332 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17446] VGAM332 gene encodes a VGAM332 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM332 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM332 precursor RNA is designated SEQ ID:318, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:318 is located at position 86054 relative to the genome of Human Herpesvirus 3.

[17447] VGAM332 precursor RNA folds onto itself, forming VGAM332 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[17448] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM332 folded precursor RNA into VGAM332 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 75%) nucleotide se-
quence of VGAM332 RNA is designated SEQ ID:3043, and
is provided hereinbelow with reference to the sequence
listing part.

[17449] VGAM332 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM332 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM332 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17450] VGAM332 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM332 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM332 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17451] The complementary binding of VGAM332 RNA, herein designated VGAM RNA, to host target binding sites on VGAM332 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM332 host target RNA into VGAM332 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17452] It is appreciated that VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM332 host target genes. The mRNA of each one of this plurality of VGAM332 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM332 RNA, herein designated VGAM RNA, and which when bound by VGAM332 RNA causes inhibition of translation of respective one or more VGAM332 host target proteins.

[17453] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM332 gene, herein designated VGAM GENE, on one or more VGAM332 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17454] It is yet further appreciated that a function of VGAM332 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM332 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM332 correlate with, and may be deduced from, the identity of the host target genes which VGAM332 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [17455] Nucleotide sequences of the VGAM332 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM332 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM332 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM332 are further described hereinbelow with reference to Table 1.
- [17456] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM332 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM332 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [17457] As mentioned hereinabove with reference to Fig. 1, a function of VGAM332 gene, herein designated VGAM is inhibition of expression of VGAM332 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM332 correlate with, and may be deduced from, the identity of the target genes which VGAM332 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17458] LOC56926 (Accession XM_052629) is a VGAM332 host target gene. LOC56926 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC56926, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC56926 BINDING SITE, designated SEQ ID:36041, to the nucleotide sequence of VGAM332 RNA, herein designated VGAM RNA, also designated SEQ ID:3043.

[17459] A function of VGAM332 is therefore inhibition of LOC56926 (Accession XM_052629). Accordingly, utilities of VGAM332 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC56926. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 333 (VGAM333) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17460] VGAM333 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM333 was detected is described hereinabove with reference to Figs. 1–8.

[17461] VGAM333 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17462] VGAM333 gene encodes a VGAM333 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM333 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM333 precursor RNA is designated SEQ ID:319, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:319 is located at position 97703 relative to the genome of Human Herpesvirus 3.

[17463] VGAM333 precursor RNA folds onto itself, forming VGAM333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17464] An enzyme complex designated DICER COMPLEX, `dices` the VGAM333 folded precursor RNA into VGAM333 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 41%) nucleotide sequence of VGAM333 RNA is designated SEQ ID:3044, and is provided hereinbelow with reference to the sequence listing part.

[17465] VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM333 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17466] VGAM333 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM333 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM333 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[17467] The complementary binding of VGAM333 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM333 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM333 host target RNA into VGAM333 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17468] It is appreciated that VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM333 host target genes. The mRNA of each one of this plurality of VGAM333 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM333 RNA, herein designated VGAM RNA, and which when bound by VGAM333 RNA causes inhibition of translation of respective one or more VGAM333 host target proteins.

[17469] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM333 gene, herein designated VGAM GENE, on one or more VGAM333 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17470] It is yet further appreciated that a function of VGAM333 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM333 correlate with, and may be deduced from, the identity of the host target genes which VGAM333 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17471] Nucleotide sequences of the VGAM333 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM333 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM333 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM333 are further described hereinbelow with reference to Table 1.

[17472] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM333 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM333 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17473] As mentioned hereinabove with reference to Fig. 1, a function of VGAM333 gene, herein designated VGAM is inhibition of expression of VGAM333 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM333 correlate with, and may be deduced from, the identity of the target genes which VGAM333 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17474] GR6 (Accession NM_007354) is a VGAM333 host target gene. GR6 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GR6, corresponding to a HOST TARGET binding site such

as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GR6 BINDING SITE, designated SEQ ID:14278, to the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17475] A function of VGAM333 is therefore inhibition of GR6 (Accession NM_007354). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GR6. Interleukin Enhancer Binding Factor 3, 90kDa (ILF3, Accession NM_004516) is another VGAM333 host target gene. ILF3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ILF3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ILF3 BINDING SITE, designated SEQ ID:10845, to the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17476] Another function of VGAM333 is therefore inhibition of Interleukin Enhancer Binding Factor 3, 90kDa (ILF3, Accession NM_004516). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases

and clinical conditions associated with ILF3. KIAA1841 (Accession XM_087056) is another VGAM333 host target gene. KIAA1841 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by KIAA1841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1841 BINDING SITE, designated SEQ ID:39027, to the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17477] Another function of VGAM333 is therefore inhibition of KIAA1841 (Accession XM_087056). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1841. pcnp (Accession NM_020357) is another VGAM333 host target gene. pcnp BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by pcnp, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of pcnp BINDING SITE, designated SEQ ID:21625, to the nucleotide sequence of

VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17478] Another function of VGAM333 is therefore inhibition of pcnp (Accession NM_020357). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with pcnp. Wingless-type MMTV Integration Site Family, Member 16 (WNT16, Accession NM_057168) is another VGAM333 host target gene. WNT16 BINDING SITE1 and WNT16 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by WNT16, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of WNT16 BINDING SITE1 and WNT16 BINDING SITE2, designated SEQ ID:27673 and SEQ ID:18169 respectively, to the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17479] Another function of VGAM333 is therefore inhibition of Wingless-type MMTV Integration Site Family, Member 16 (WNT16, Accession NM_057168). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with WNT16.

LOC139770 (Accession XM_060053) is another VGAM333 host target gene. LOC139770 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC139770, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC139770 BINDING SITE, designated SEQ ID:37147, to the nucleotide sequence of VGAM333 RNA, herein designated VGAM RNA, also designated SEQ ID:3044.

[17480] Another function of VGAM333 is therefore inhibition of LOC139770 (Accession XM_060053). Accordingly, utilities of VGAM333 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC139770. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 334 (VGAM334) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17481] VGAM334 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The

method by which VGAM334 was detected is described hereinabove with reference to Figs. 1–8.

[17482] VGAM334 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Human Herpesvirus 3. VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17483] VGAM334 gene encodes a VGAM334 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM334 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM334 precursor RNA is designated SEQ ID:320, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:320 is located at position 97885 relative to the genome of Human Herpesvirus 3.

[17484] VGAM334 precursor RNA folds onto itself, forming VGAM334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence

of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17485] An enzyme complex designated DICER COMPLEX, `dices` the VGAM334 folded precursor RNA into VGAM334 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 86%) nucleotide sequence of VGAM334 RNA is designated SEQ ID:3045, and is provided hereinbelow with reference to the sequence listing part.

[17486] VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM334 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17487] VGAM334 RNA, herein designated VGAM RNA, binds com-

plementarily to one or more host target binding sites located in untranslated regions of VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM334 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM334 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3'UTR region, this is meant as an example only – these host target binding sites may be located in the 3'UTR region, the 5'UTR region, or in both 3'UTR and 5'UTR regions.

[17488] The complementary binding of VGAM334 RNA, herein designated VGAM RNA, to host target binding sites on

VGAM334 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM334 host target RNA into VGAM334 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17489] It is appreciated that VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM334 host target genes. The mRNA of each one of this plurality of VGAM334 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM334 RNA, herein designated VGAM RNA, and which when bound by VGAM334 RNA causes inhibition of translation of respective one or more VGAM334 host target proteins.

[17490] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM334 gene, herein designated VGAM GENE, on one or more VGAM334 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove

with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17491] It is yet further appreciated that a function of VGAM334 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of viral infection by Human Herpesvirus 3. Specific functions, and accordingly utilities, of VGAM334 correlate with, and may be deduced from, the identity of the host target genes which VGAM334 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17492] Nucleotide sequences of the VGAM334 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM334 RNA, herein designated VGAM RNA,

and a schematic representation of the secondary folding of VGAM334 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM334 are further described hereinbelow with reference to Table 1.

[17493] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM334 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM334 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17494] As mentioned hereinabove with reference to Fig. 1, a function of VGAM334 gene, herein designated VGAM is inhibition of expression of VGAM334 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM334 correlate with, and may be deduced from, the identity of the target genes which VGAM334 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17495] ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933) is a VGAM334 host target gene. ATP8B2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ATP8B2, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ATP8B2 BINDING SITE, designated SEQ ID:32518, to the nucleotide sequence of VGAM334 RNA, herein designated VGAM RNA, also designated SEQ ID:3045.

[17496] A function of VGAM334 is therefore inhibition of ATPase, Class I, Type 8B, Member 2 (ATP8B2, Accession XM_036933). Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ATP8B2. Very Low Density Lipoprotein Receptor (VLDLR, Accession XM_045386) is another VGAM334 host target gene. VLDLR BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by VLDLR, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VLDLR BINDING SITE, designated SEQ ID:34449, to the nucleotide sequence of VGAM334 RNA, herein designated VGAM RNA, also designated SEQ ID:3045.

[17497] Another function of VGAM334 is therefore inhibition of Very Low Density Lipoprotein Receptor (VLDLR, Accession

XM_045386), a gene which may play a crucial role in triglyceride metabolism. Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VLDLR. The function of VLDLR and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM103. KIAA1026 (Accession XM_048825) is another VGAM334 host target gene. KIAA1026 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1026, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1026 BINDING SITE, designated SEQ ID:35273, to the nucleotide sequence of VGAM334 RNA, herein designated VGAM RNA, also designated SEQ ID:3045.

[17498] Another function of VGAM334 is therefore inhibition of KIAA1026 (Accession XM_048825). Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1026. LOC135818 (Accession XM_059804) is another VGAM334 host target gene. LOC135818 BINDING SITE is

HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC135818, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC135818 BINDING SITE, designated SEQ ID:37094, to the nucleotide sequence of VGAM334 RNA, herein designated VGAM RNA, also designated SEQ ID:3045.

[17499] Another function of VGAM334 is therefore inhibition of LOC135818 (Accession XM_059804). Accordingly, utilities of VGAM334 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC135818. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 335 (VGAM335) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17500] VGAM335 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM335 was detected is described hereinabove with reference to Figs. 1-8.

[17501] VGAM335 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17502] VGAM335 gene encodes a VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM335 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM335 precursor RNA is designated SEQ ID:321, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:321 is located at position 23128 relative to the genome of Saimiriine Herpesvirus 2.

[17503] VGAM335 precursor RNA folds onto itself, forming VGAM335 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nu-

cleotide sequence of the second half thereof.

[17504] An enzyme complex designated DICER COMPLEX, `dices` the VGAM335 folded precursor RNA into VGAM335 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 71%) nucleotide sequence of VGAM335 RNA is designated SEQ ID:3046, and is provided hereinbelow with reference to the sequence listing part.

[17505] VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM335 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17506] VGAM335 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM335 host target

RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM335 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM335 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17507] The complementary binding of VGAM335 RNA, herein designated VGAM RNA, to host target binding sites on VGAM335 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and

BINDING SITE III, inhibits translation of VGAM335 host target RNA into VGAM335 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17508] It is appreciated that VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM335 host target genes. The mRNA of each one of this plurality of VGAM335 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM335 RNA, herein designated VGAM RNA, and which when bound by VGAM335 RNA causes inhibition of translation of respective one or more VGAM335 host target proteins.

[17509] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM335 gene, herein designated VGAM GENE, on one or more VGAM335 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated

only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17510] It is yet further appreciated that a function of VGAM335 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM335 correlate with, and may be deduced from, the identity of the host target genes which VGAM335 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17511] Nucleotide sequences of the VGAM335 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM335 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM335 folded precursor RNA, herein designated

VGAM FOLDED PRECURSOR RNA, of VGAM335 are further described hereinbelow with reference to Table 1.

[17512] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM335 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM335 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17513] As mentioned hereinabove with reference to Fig. 1, a function of VGAM335 gene, herein designated VGAM is inhibition of expression of VGAM335 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM335 correlate with, and may be deduced from, the identity of the target genes which VGAM335 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17514] Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM_000499) is a VGAM335 host target gene. CYP1A1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CYP1A1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BIND-

ING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CYP1A1 BINDING SITE, designated SEQ ID:6114, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17515] A function of VGAM335 is therefore inhibition of Cytochrome P450, Subfamily I (aromatic compound-inducible), Polypeptide 1 (CYP1A1, Accession NM_000499), a gene which intervenes in an NADPH-dependent electron transport pathway. Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CYP1A1. The function of CYP1A1 has been established by previous studies. Polycyclic aromatic hydrocarbons (PAHs) generated from the combustion of fossil fuels, and aromatic amines, which are present in cigarette smoke and other environmental media, present 2 classic environmental carcinogens. Perera (1997) reviewed evidence on variation and susceptibility to the effects of these carcinogens. CYP1A1 encodes a phase I cytochrome P450 enzyme that metabolizes PAHs such as benzo[a]pyrene (BP). About 10% of Caucasians have a highly inducible form of the enzyme that is associated with an increased risk of lung cancer in

smokers. Although not all studies have been positive, in Japanese and certain Caucasian populations, increased lung cancer risk was correlated with 1 or both CYP1A1 polymorphisms: the so called MSPI polymorphism and the closely-linked exon 7 (isoleucine-valine) polymorphism (Kawajiri et al., 1996; Nakachi et al., 1991; Xu et al., 1996). The greatest incremental lung cancer risk from the 'susceptible' CYP1A1 genotype was seen in light smokers (7 times the risk of light smokers without the genotype), whereas heavy smokers with this genotype had less than twice the risk of heavy smokers without the genotype. The proposed mechanism for the increased risk is higher CYP1A1 inducibility or enhanced catalytic activity of the valine-type CYP1A1 enzyme. Consistent with these mechanisms, Mooney et al. (1997) found that U. S. smoking volunteers with the exon 7 mutation had more PAH-DNA adducts in their white blood cells than did smokers without the variant. Perera (1997) stated that PAH-DNA adducts were also elevated in cord blood and placenta of newborns with the CYP1A1 MSP1 polymorphism, which suggested that the genetic polymorphism may increase risk from transplacental PAH exposure. In lung tissue of adults, adduct concentration correlated with CYP1A1 ex-

pression or enzyme activity. Perera (1997) noted that lung tumors of Japanese smokers were found to be significantly more likely to have p53 (OMIM Ref. No. 191170) mutations if they had the susceptible CYP1A1 genotype. A failure to demonstrate genetic susceptibility through CYP1A1 polymorphism when exposure to the environmental carcinogen is heavy is observed with some other polymorphisms and carcinogenic exposures. It is possible that at higher exposures, the effects of the genetic traits are overwhelmed by the environmental insults. Numerous studies have shown that maternal cigarette smoking during pregnancy is associated with reduced birthweight and increased risk of low birthweight, defined as weight less than 2,500 g. Maternal cigarette smoking has thus been identified as the single largest modifiable risk factor for intrauterine growth restriction in developed countries. However, not all women who smoke cigarettes during pregnancy have low-birthweight infants. Wang et al. (2002) studied whether the association between maternal cigarette smoking and infant birthweight differs by polymorphisms of 2 maternal metabolic genes: CYP1A1 and GSTT1 (OMIM Ref. No. 600436). The CYP1A1 polymorphism was the Msp1 polymorphism (AA vs Aa and aa); the

GSTT1 polymorphism was present versus absent. Wang et al. (2002) found that regardless of genotype, continuous maternal smoking during pregnancy was associated with a mean reduction of 377 g in birthweight. They found that for the CYP1A1 genotype, the estimated reduction in birthweight was 252 g for the AA genotype group, but was 520 g for the Aa/aa genotype group. For the GSTT1 genotype, they found the estimated reduction in birthweight was 285 g and 642 g for the present and absent genotype groups, respectively. When both CYP1A1 and GSTT1 genotypes were considered, Wang et al. (2002) found the greatest reduction in birthweight among smoking mothers with the CYP1A1 Aa/aa and GSTT1 absent genotypes. Among mothers who had not smoked during their pregnancy or during the 3 months prior to their pregnancy, genotype did not independently confer an adverse effect. Animal model experiments lend further support to the function of CYP1A1. Thum and Borlak (2000) investigated the gene expression of major human cytochrome P450 genes in various regions of explanted hearts from 6 patients with dilated cardiomyopathy and 1 with transposition of the arterial trunk and 2 samples of normal heart. mRNA for cytochrome 1A1 was predomi-

nantly expressed in the right ventricle. A strong correlation between tissue-specific gene expression and enzyme activity was found. Thum and Borlak (2000) concluded that their findings showed that expression of genes for cytochrome P450 monooxygenases and verapamil metabolism are found predominantly in the right side of the heart, and suggested that this observation may explain the lack of efficacy of certain cardioselective drugs.

[17516] It is appreciated that the abovementioned animal model for CYP1A1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17517] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17518] Corchero, J.; Pimprale, S.; Kimura, S.; Gonzalez, F. J. : Organization of the CYP1A cluster on human chromosome 15: implications for gene regulation. Pharmacogenetics 11: 1-6, 2001. ; and

[17519] Petersen, D. D.; McKinney, C. E.; Ikeya, K.; Smith, H. H.; Bale, A. E.; McBride, O. W.; Nebert, D. W. : Human CYP1A1 gene: cosegregation of the enzyme inducibility phenotype and an RFL.

[17520] Further studies establishing the function and utilities of CYP1A1 are found in John Hopkins OMIM database record ID 108330, and in cited publications numbered 12082–12087, 788, 848–852, 11777–861, 12760, 12761–86 and 3429–869 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Protein Phosphatase 2, Regulatory Subunit B (B56), Gamma Isoform (PPP2R5C, Accession NM_002719) is another VGAM335 host target gene. PPP2R5C BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by PPP2R5C, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PPP2R5C BINDING SITE, designated SEQ ID:8588, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17521] Another function of VGAM335 is therefore inhibition of Protein Phosphatase 2, Regulatory Subunit B (B56), Gamma Isoform (PPP2R5C, Accession NM_002719), a gene which is a regulatory subunit of protein phosphatase 2A. Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions

associated with PPP2R5C. The function of PPP2R5C has been established by previous studies. Protein phosphorylation is a regulatory mechanism commonly employed in cellular processes such as cell cycle progression, growth factor signaling, and cell transformation. Protein phosphatase 2A (PP2A), a heterotrimeric serine/threonine phosphatase, has been implicated in a variety of regulatory processes including cell growth and division, muscle contraction, and gene transcription. PP2A is a trimeric enzyme composed of a catalytic subunit (OMIM Ref. No. 176915), a structural subunit, and any of several different regulatory subunits which control its specificity. One family of related PP2A regulatory subunits is designated the B56 family and contains at least 5 different members (McCright and Virshup (1995)). The alpha (OMIM Ref. No. 601643) and gamma subunits are expressed at highest levels in skeletal and cardiac muscle. Both the delta (OMIM Ref. No. 601646) and gamma subunits encode nuclear phosphoproteins and at least 3 splice variants of the gamma subunit have been reported. The longest gamma isoform is a phosphoprotein, but the shortest is not.

[17522] Full details of the abovementioned studies are described in the following publications, the disclosure of which are

hereby incorporated by reference:

- [17523] McCright, B.; Brothman, A. R.; Virshup, D. M. : Assignment of human protein phosphatase 2A regulatory subunit genes B56-alpha, B56-beta, B56-gamma, B56-delta, and B56-epsilon (PPP2R5A--PPP2R5E), highly expressed in muscle and brain, to chromosome regions 1q41, 11q12, 3p21, 6p21.1, and 7p11.2-to-p12. Genomics 36: 168-170, 1996. ; and
- [17524] McCright, B.; Virshup, D. M. : Identification of a new family of protein phosphatase 2A regulatory subunits. J. Biol. Chem. 270: 26123-26128, 1995.
- [17525] Further studies establishing the function and utilities of PPP2R5C are found in John Hopkins OMIM database record ID 601645, and in cited publications numbered 6687-668 and 6554 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. ALDH9 (Accession NM_000696) is another VGAM335 host target gene. ALDH9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by ALDH9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ALDH9 BINDING SITE, designated SEQ

ID:6360, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17526] Another function of VGAM335 is therefore inhibition of ALDH9 (Accession NM_000696). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ALDH9. Basic Helix-loop-helix Domain Containing, Class B, 2 (BHLHB2, Accession NM_003670) is another VGAM335 host target gene. BHLHB2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BHLHB2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BHLHB2 BINDING SITE, designated SEQ ID:9753, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17527] Another function of VGAM335 is therefore inhibition of Basic Helix-loop-helix Domain Containing, Class B, 2 (BHLHB2, Accession NM_003670). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BHLHB2.

Chromosome 21 Open Reading Frame 41 (C21orf41, Accession NM_138332) is another VGAM335 host target gene. C21orf41 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by C21orf41, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C21orf41 BINDING SITE, designated SEQ ID:28732, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17528] Another function of VGAM335 is therefore inhibition of Chromosome 21 Open Reading Frame 41 (C21orf41, Accession NM_138332). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C21orf41. DKFZP564D206 (Accession XM_166501) is another VGAM335 host target gene. DKFZP564D206 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP564D206, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DK-

FZP564D206 BINDING SITE, designated SEQ ID:44428, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17529] Another function of VGAM335 is therefore inhibition of DKFZP564D206 (Accession XM_166501). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564D206. DKFZP761D0211 (Accession NM_032039) is another VGAM335 host target gene. DKFZP761D0211 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP761D0211, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP761D0211 BINDING SITE, designated SEQ ID:25737, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17530] Another function of VGAM335 is therefore inhibition of DKFZP761D0211 (Accession NM_032039). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP761D0211. FLJ12649 (Accession NM_024597)

is another VGAM335 host target gene. FLJ12649 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ12649, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ12649 BINDING SITE, designated SEQ ID:23834, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17531] Another function of VGAM335 is therefore inhibition of FLJ12649 (Accession NM_024597). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ12649. FLJ13441 (Accession NM_023924) is another VGAM335 host target gene. FLJ13441 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13441, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13441 BINDING SITE, designated SEQ ID:23399, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17532] Another function of VGAM335 is therefore inhibition of FLJ13441 (Accession NM_023924). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13441. MGC2306 (Accession NM_032638) is another VGAM335 host target gene. MGC2306 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC2306, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC2306 BINDING SITE, designated SEQ ID:26357, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17533] Another function of VGAM335 is therefore inhibition of MGC2306 (Accession NM_032638). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC2306. MGC26684 (Accession NM_144568) is another VGAM335 host target gene. MGC26684 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC26684, corresponding to a HOST TARGET binding site such as BINDING SITE I,

BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26684 BINDING SITE, designated SEQ ID:29372, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17534] Another function of VGAM335 is therefore inhibition of MGC26684 (Accession NM_144568). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26684. SCYA28 (Accession NM_019846) is another VGAM335 host target gene. SCYA28 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SCYA28, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SCYA28 BINDING SITE, designated SEQ ID:21250, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17535] Another function of VGAM335 is therefore inhibition of SCYA28 (Accession NM_019846). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SCYA28.

LOC152627 (Accession XM_087495) is another VGAM335 host target gene. LOC152627 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC152627, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC152627 BINDING SITE, designated SEQ ID:39298, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17536] Another function of VGAM335 is therefore inhibition of LOC152627 (Accession XM_087495). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC152627. LOC153937 (Accession XM_087813) is another VGAM335 host target gene. LOC153937 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC153937, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC153937 BINDING SITE, designated SEQ ID:39448, to the nucleotide sequence of VGAM335 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3046.

[17537] Another function of VGAM335 is therefore inhibition of LOC153937 (Accession XM_087813). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC153937. LOC200609 (Accession XM_117256) is another VGAM335 host target gene. LOC200609 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC200609, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC200609 BINDING SITE, designated SEQ ID:43335, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17538] Another function of VGAM335 is therefore inhibition of LOC200609 (Accession XM_117256). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC200609. LOC92249 (Accession XM_043814) is another VGAM335 host target gene. LOC92249 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC92249, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC92249 BINDING SITE, designated SEQ ID:34025, to the nucleotide sequence of VGAM335 RNA, herein designated VGAM RNA, also designated SEQ ID:3046.

[17539] Another function of VGAM335 is therefore inhibition of LOC92249 (Accession XM_043814). Accordingly, utilities of VGAM335 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC92249. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 336 (VGAM336) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17540] VGAM336 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM336 was detected is described hereinabove with reference to Figs. 1–8.

[17541] VGAM336 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2.

VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17542] VGAM336 gene encodes a VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM336 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM336 precursor RNA is designated SEQ ID:322, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:322 is located at position 23007 relative to the genome of Saimiriine Herpesvirus 2.

[17543] VGAM336 precursor RNA folds onto itself, forming VGAM336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17544] An enzyme complex designated DICER COMPLEX, `dices`

the VGAM336 folded precursor RNA into VGAM336 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 55%) nucleotide sequence of VGAM336 RNA is designated SEQ ID:3047, and is provided hereinbelow with reference to the sequence listing part.

[17545] VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM336 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17546] VGAM336 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nu-

cleotide sequence of VGAM336 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM336 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17547] The complementary binding of VGAM336 RNA, herein designated VGAM RNA, to host target binding sites on VGAM336 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM336 host target RNA into VGAM336 host target protein, herein desig-

nated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17548] It is appreciated that VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM336 host target genes. The mRNA of each one of this plurality of VGAM336 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM336 RNA, herein designated VGAM RNA, and which when bound by VGAM336 RNA causes inhibition of translation of respective one or more VGAM336 host target proteins.

[17549] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM336 gene, herein designated VGAM GENE, on one or more VGAM336 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are

also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17550] It is yet further appreciated that a function of VGAM336 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM336 correlate with, and may be deduced from, the identity of the host target genes which VGAM336 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17551] Nucleotide sequences of the VGAM336 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM336 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM336 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM336 are further described hereinbelow with reference to Table 1.

[17552] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM336 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM336 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17553] As mentioned hereinabove with reference to Fig. 1, a function of VGAM336 gene, herein designated VGAM is inhibition of expression of VGAM336 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM336 correlate with, and may be deduced from, the identity of the target genes which VGAM336 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17554] ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM_001089) is a VGAM336 host target gene. ABCA3 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by ABCA3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of ABCA3 BINDING SITE, designated SEQ

ID:6745, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17555] A function of VGAM336 is therefore inhibition of ATP-binding Cassette, Sub-family A (ABC1), Member 3 (ABCA3, Accession NM_001089), a gene which may be a transporter, may act as an efflux pump for chemotherapeutics drugs. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with ABCA3. The function of ABCA3 has been established by previous studies. Klugbauer and Hofmann (1996) isolated cDNA clones encoding a novel protein they designated ABC-C from a human medullary thyroid cancer cell line. ABC-C has typical structural features of the ABC transporter family (see OMIM Ref. No. 600046). They determined that the transporter consists of a 1,704-amino acid polypeptide with 2 homologous repeats, each harboring 6 putative transmembrane helices and an ATP-binding cassette motif. The ABC-C protein showed approximately 50% homology with the MRP1 (OMIM Ref. No. 158343) protein. Klugbauer and Hofmann (1996) mapped the ABC-C gene (also symbolized ABC3) to chromosome 16p13.3 by comparison with an identical

cDNA clone mapping to that chromosomal region. They noted that the ABC-C gene and the gene encoding MRP1 map within the same chromosomal band. Wu and Horvitz (1998) found that the *C. elegans* protein ced-7 is homologous to human ABC3. Ced-7 functions in the engulfment of cell corpses during programmed cell death, is broadly expressed during embryogenesis, and is localized to the plasma membrane. Mosaic analysis revealed that ced-7 functions in both dying cells and engulfing cells during the engulfment process. Wu and Horvitz (1998) proposed that ced-7 functions to translocate molecules that mediate homotypic adhesion between the cell surfaces of the dying and engulfing cells. They also suggested that ABC3 may be functionally similar and that the molecular mechanism underlying cell corpse engulfment during programmed cell death may be conserved from nematodes to mammals.

[17556] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17557] Klugbauer, N.; Hofmann, F. : Primary structure of a novel ABC transporter with a chromosomal localization on the band encoding the multidrug resistance-associated pro-

tein. FEBS Lett. 391: 61–65, 1996. ; and

[17558] Wu, Y.-C.; Horvitz, H. R. : The C. elegans cell corpse engulfment gene ced-7 encodes a protein similar to ABC transporters. Cell 93: 951–960, 1998.

[17559] Further studies establishing the function and utilities of ABCA3 are found in John Hopkins OMIM database record ID 601615, and in cited publications numbered 1246–1248 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812) is another VGAM336 host target gene. BAALC BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by BAALC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BAALC BINDING SITE, designated SEQ ID:24193, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17560] Another function of VGAM336 is therefore inhibition of Brain and Acute Leukemia, Cytoplasmic (BAALC, Accession NM_024812). Accordingly, utilities of VGAM336 include

diagnosis, prevention and treatment of diseases and clinical conditions associated with BAALC. Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM_000131) is another VGAM336 host target gene. F7 BINDING SITE1 and F7 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by F7, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of F7 BINDING SITE1 and F7 BINDING SITE2, designated SEQ ID:5609 and SEQ ID:21238 respectively, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17561] Another function of VGAM336 is therefore inhibition of Coagulation Factor VII (serum prothrombin conversion accelerator) (F7, Accession NM_000131). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with F7. Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269) is another VGAM336 host target gene. LEF1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LEF1, corre-

sponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LEF1 BINDING SITE, designated SEQ ID:18390, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17562] Another function of VGAM336 is therefore inhibition of Lymphoid Enhancer-binding Factor 1 (LEF1, Accession NM_016269), a gene which plays an essential role in the formation of several organs and structures that require inductive tissue interactions. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LEF1. The function of LEF1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM200. Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM_003889) is another VGAM336 host target gene. NR1I2 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by NR1I2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of NR1I2 BINDING SITE, designated SEQ ID:9971, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17563] Another function of VGAM336 is therefore inhibition of Nuclear Receptor Subfamily 1, Group I, Member 2 (NR1I2, Accession NM_003889), a gene which binds to a response element in the cyp3a4 gene promoter and activates its expression in response to a wide variety of endobiotics and xenobiotics. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NR1I2. The function of NR1I2 has been established by previous studies. Lehmann et al. (1998) identified a nuclear receptor, termed PXR, that binds to the rifampicin/dexamethasone response element in the CYP3A4 (OMIM Ref. No. 124010) promoter as a heterodimer with the 9-cis retinoic acid receptor RXR (see OMIM Ref. No. 180245). The human PXR is related to the mouse Pxr1, which they had cloned and shown to be activated by dexamethasone, pregnenolone 16- α -carbonitrile (PCN), and other compounds known to induce expression of the CYP3A1 gene, the predominant form of CYP3A in rat liver and intestine. Lehmann et

al. (1998) isolated PXR clones from a human liver cDNA library. Amino acid sequence comparison showed that human PXR shared 96% and 76% sequence identity with mouse Pxr1 in the DNA-binding and ligand-binding domains, respectively. Initiation of translation at a CUG initiation codon would yield a protein of 434 amino acids. Northern blot analysis detected most abundant expression in liver, colon, and small intestine; transcripts of 2.6, 4.3, and 5 kb were present in each of these tissues. Lehmann et al. (1998) provided several lines of evidence indicating that human PXR serves as a key transcriptional regulator of the CYP3A4 gene. Animal model experiments lend further support to the function of NR1I2. The induction of CYP3A enzymes is species-specific and believed to involve 1 or more cellular factors, or receptor-like xenosensors. Xie et al. (2000) identified one such factor as the nuclear receptor Pxr and its human homolog SXR. Xie et al. (2000) showed that targeted disruption of the mouse Pxr gene abolished induction of CYP3A by prototypic inducers such as dexamethasone or pregnenolone-16- α -carbonitrile. In Pxr-null mice carrying a transgene for an activated form of human SXR, there was constitutive upregulation of CYP3A gene expression and en-

hanced protection against toxic xenobiotic compounds. Xie et al. (2000) demonstrated that species origin of the receptor, rather than the promoter structure of the CYP3A genes, dictates the species-specific pattern of CYP3A inducibility. Thus, they could generate 'humanized' transgenic mice that were responsive to human-specific inducers such as the antibiotic rifampicin. Xie et al. (2000) concluded that the SXR/Pxr genes encode the primary species-specific xenosensors that mediate the adaptive hepatic response, and may represent the critical biochemical mechanism of human xenoprotection.

[17564] It is appreciated that the abovementioned animal model for NR1I2 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17565] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17566] Lehmann, J. M.; McKee, D. D.; Watson, M. A.; Willson, T. M.; Moore, J. T.; Kliewer, S. A. : The human orphan nuclear receptor PXR is activated by compounds that regulate CYP3A4 gene expression and cause drug interactions. J. Clin. Invest. 102: 1016–1023, 1998. ; and

[17567] Xie, W.; Barwick, J. L.; Downes, M.; Blumberg, B.; Simon, C. M.; Nelson, M. C.; Neuschwander-Tetri, B. A.; Brunt, E. M.; Guzelian, P. S.; Evans, R. M. : Humanized xenobiotic response in.

[17568] Further studies establishing the function and utilities of NR1I2 are found in John Hopkins OMIM database record ID 603065, and in cited publications numbered 8483–8484, 3423, 3882, 848 and 8577 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630) is another VGAM336 host target gene. SLC21A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC21A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC21A2 BINDING SITE, designated SEQ ID:12156, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17569] Another function of VGAM336 is therefore inhibition of Solute Carrier Family 21 (prostaglandin transporter), Member 2 (SLC21A2, Accession NM_005630), a gene

which is a Prostaglandin transporter. Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC21A2. The function of SLC21A2 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM83. BCAA (Accession NM_016374) is another VGAM336 host target gene. BCAA BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by BCAA, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of BCAA BINDING SITE, designated SEQ ID:18513, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17570] Another function of VGAM336 is therefore inhibition of BCAA (Accession NM_016374). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with BCAA. Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749) is another VGAM336 host target gene. C20orf139 BINDING SITE is HOST TARGET binding

site found in the 3` untranslated region of mRNA encoded by C20orf139, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of C20orf139 BINDING SITE, designated SEQ ID:41104, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17571] Another function of VGAM336 is therefore inhibition of Chromosome 20 Open Reading Frame 139 (C20orf139, Accession XM_097749). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with C20orf139. Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273) is another VGAM336 host target gene. CHST3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by CHST3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CHST3 BINDING SITE, designated SEQ ID:10486, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ

ID:3047.

[17572] Another function of VGAM336 is therefore inhibition of Carbohydrate (chondroitin 6) Sulfotransferase 3 (CHST3, Accession NM_004273). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CHST3. DKFZP434D146 (Accession NM_015595) is another VGAM336 host target gene. DKFZP434D146 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DKFZP434D146, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434D146 BINDING SITE, designated SEQ ID:17872, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17573] Another function of VGAM336 is therefore inhibition of DKFZP434D146 (Accession NM_015595). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434D146. DKFZP434H132 (Accession NM_015492) is another VGAM336 host target gene. DKFZP434H132 BINDING SITE is HOST TARGET binding site

found in the 3' untranslated region of mRNA encoded by DKFZP434H132, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP434H132 BINDING SITE, designated SEQ ID:17761, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17574] Another function of VGAM336 is therefore inhibition of DKFZP434H132 (Accession NM_015492). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP434H132. FLJ13902 (Accession NM_024653) is another VGAM336 host target gene. FLJ13902 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ13902, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ13902 BINDING SITE, designated SEQ ID:23951, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17575] Another function of VGAM336 is therefore inhibition of

FLJ13902 (Accession NM_024653). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ13902. FLJ14936 (Accession NM_032284) is another VGAM336 host target gene. FLJ14936 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ14936, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ14936 BINDING SITE, designated SEQ ID:26042, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17576] Another function of VGAM336 is therefore inhibition of FLJ14936 (Accession NM_032284). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ14936. FLJ20337 (Accession NM_017772) is another VGAM336 host target gene. FLJ20337 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ20337, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity

of the nucleotide sequences of FLJ20337 BINDING SITE, designated SEQ ID:19392, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17577] Another function of VGAM336 is therefore inhibition of FLJ20337 (Accession NM_017772). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20337. FLJ20689 (Accession NM_017972) is another VGAM336 host target gene. FLJ20689 BINDING SITE1 and FLJ20689 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by FLJ20689, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ20689 BINDING SITE1 and FLJ20689 BINDING SITE2, designated SEQ ID:19702 and SEQ ID:19598 respectively, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17578] Another function of VGAM336 is therefore inhibition of FLJ20689 (Accession NM_017972). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ20689.

LBP-9 (Accession NM_014553) is another VGAM336 host target gene. LBP-9 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LBP-9, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LBP-9 BINDING SITE, designated SEQ ID:15877, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17579] Another function of VGAM336 is therefore inhibition of LBP-9 (Accession NM_014553). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LBP-9. MGC26684 (Accession NM_144568) is another VGAM336 host target gene. MGC26684 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MGC26684, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26684 BINDING SITE, designated SEQ ID:29371, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA,

also designated SEQ ID:3047.

[17580] Another function of VGAM336 is therefore inhibition of MGC26684 (Accession NM_144568). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26684. MGC26744 (Accession NM_144645) is another VGAM336 host target gene. MGC26744 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by MGC26744, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MGC26744 BINDING SITE, designated SEQ ID:29471, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17581] Another function of VGAM336 is therefore inhibition of MGC26744 (Accession NM_144645). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MGC26744. Protein Regulator of Cytokinesis 1 (PRC1, Accession NM_003981) is another VGAM336 host target gene. PRC1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by

PRC1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PRC1 BINDING SITE, designated SEQ ID:10119, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17582] Another function of VGAM336 is therefore inhibition of Protein Regulator of Cytokinesis 1 (PRC1, Accession NM_003981). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with PRC1. Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617) is another VGAM336 host target gene. SLC11A2 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SLC11A2, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SLC11A2 BINDING SITE, designated SEQ ID:6222, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17583] Another function of VGAM336 is therefore inhibition of

Solute Carrier Family 11 (proton-coupled divalent metal ion transporters), Member 2 (SLC11A2, Accession NM_000617). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SLC11A2. VRP (Accession NM_007063) is another VGAM336 host target gene. VRP BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by VRP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of VRP BINDING SITE, designated SEQ ID:13925, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17584] Another function of VGAM336 is therefore inhibition of VRP (Accession NM_007063). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with VRP. LOC112840 (Accession NM_080666) is another VGAM336 host target gene. LOC112840 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC112840, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE

II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC112840 BINDING SITE, designated SEQ ID:27955, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17585] Another function of VGAM336 is therefore inhibition of LOC112840 (Accession NM_080666). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC112840. LOC122970 (Accession XM_058672) is another VGAM336 host target gene. LOC122970 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC122970, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC122970 BINDING SITE, designated SEQ ID:36713, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17586] Another function of VGAM336 is therefore inhibition of LOC122970 (Accession XM_058672). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

LOC122970. LOC145955 (Accession XM_096912) is another VGAM336 host target gene. LOC145955 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC145955, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC145955 BINDING SITE, designated SEQ ID:40641, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17587] Another function of VGAM336 is therefore inhibition of LOC145955 (Accession XM_096912). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC145955. LOC146481 (Accession XM_085484) is another VGAM336 host target gene. LOC146481 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146481, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146481 BINDING SITE, designated SEQ ID:38174, to the nucleotide sequence of VGAM336 RNA, herein desig-

nated VGAM RNA, also designated SEQ ID:3047.

[17588] Another function of VGAM336 is therefore inhibition of LOC146481 (Accession XM_085484). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146481. LOC146957 (Accession XM_085652) is another VGAM336 host target gene. LOC146957 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC146957, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC146957 BINDING SITE, designated SEQ ID:38280, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17589] Another function of VGAM336 is therefore inhibition of LOC146957 (Accession XM_085652). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC146957. LOC204084 (Accession XM_115181) is another VGAM336 host target gene. LOC204084 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC204084, cor-

responding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC204084 BINDING SITE, designated SEQ ID:43083, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17590] Another function of VGAM336 is therefore inhibition of LOC204084 (Accession XM_115181). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC204084. LOC253841 (Accession XM_172811) is another VGAM336 host target gene. LOC253841 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC253841, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC253841 BINDING SITE, designated SEQ ID:46091, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17591] Another function of VGAM336 is therefore inhibition of LOC253841 (Accession XM_172811). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC253841. LOC254173 (Accession XM_173022) is another VGAM336 host target gene. LOC254173 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC254173, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC254173 BINDING SITE, designated SEQ ID:46287, to the nucleotide sequence of VGAM336 RNA, herein designated VGAM RNA, also designated SEQ ID:3047.

[17592] Another function of VGAM336 is therefore inhibition of LOC254173 (Accession XM_173022). Accordingly, utilities of VGAM336 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC254173. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 337 (VGAM337) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17593] VGAM337 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM337 was detected is described hereinabove with reference to Figs. 1–8.

[17594] VGAM337 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17595] VGAM337 gene encodes a VGAM337 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM337 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM337 precursor RNA is designated SEQ ID:323, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:323 is located at position 22516 relative to the genome of Saimiriine Herpesvirus 2.

[17596] VGAM337 precursor RNA folds onto itself, forming VGAM337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17597] An enzyme complex designated DICER COMPLEX, `dices` the VGAM337 folded precursor RNA into VGAM337 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 81%) nucleotide sequence of VGAM337 RNA is designated SEQ ID:3048, and is provided hereinbelow with reference to the sequence listing part.

[17598] VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM337 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17599] VGAM337 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM337 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM337 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17600] The complementary binding of VGAM337 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM337 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM337 host target RNA into VGAM337 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17601] It is appreciated that VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM337 host target genes. The mRNA of each one of this plurality of VGAM337 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM337 RNA, herein designated VGAM RNA, and which when bound by VGAM337 RNA causes inhibition of translation of respective one or more VGAM337 host target proteins.

[17602] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM337 gene, herein designated VGAM GENE, on one or more VGAM337 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17603] It is yet further appreciated that a function of VGAM337 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM337 correlate with, and may be deduced from, the identity of the host target genes which VGAM337 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17604] Nucleotide sequences of the VGAM337 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM337 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM337 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM337 are further described hereinbelow with reference to Table 1.

[17605] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM337 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM337 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17606] As mentioned hereinabove with reference to Fig. 1, a function of VGAM337 gene, herein designated VGAM is inhibition of expression of VGAM337 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM337 correlate with, and may be deduced from, the identity of the target genes which VGAM337 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17607] Copine III (CPNE3, Accession NM_003909) is a VGAM337 host target gene. CPNE3 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA

encoded by CPNE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CPNE3 BINDING SITE, designated SEQ ID:9997, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17608] A function of VGAM337 is therefore inhibition of Copine III (CPNE3, Accession NM_003909), a gene which may function in membrane trafficking. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CPNE3. The function of CPNE3 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM28. Dystonia 1, Torsion (autosomal dominant; torsin A) (DYT1, Accession NM_000113) is another VGAM337 host target gene. DYT1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DYT1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DYT1 BINDING SITE,

designated SEQ ID:5577, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17609] Another function of VGAM337 is therefore inhibition of Dystonia 1, Torsion (autosomal dominant; torsin A) (DYT1, Accession NM_000113). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DYT1. UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminyl)-galactosylglucosylceramide N-acetylgalactosaminyltransferase (GalNAc-T) (GALGT, Accession NM_001478) is another VGAM337 host target gene. GALGT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by GALGT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GALGT BINDING SITE, designated SEQ ID:7214, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ

ID:3048.

[17610] Another function of VGAM337 is therefore inhibition of UDP-N-acetyl-alpha-D-galactosamine:(N-acetylneuraminyl)-galactosylglucosylceramide N-acetylgalactosaminyltransferase (GalNAc-T) (GALGT, Accession NM_001478), a gene which is involved in the biosynthesis of gangliosides gm2, gd2 and ga2. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GALGT. The function of GALGT and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM179. Reticulon 1 (RTN1, Accession NM_021136) is another VGAM337 host target gene. RTN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RTN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide se-

quences of RTN1 BINDING SITE, designated SEQ ID:22110, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17611] Another function of VGAM337 is therefore inhibition of Reticulon 1 (RTN1, Accession NM_021136), a gene which may be involved in neuroendocrine secretion or in membrane – membrane trafficking in neuroendocrine cells. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RTN1. The function of RTN1 has been established by previous studies. Roebroek et al. (1993) described the cloning of a gene that encodes a group of neuroendocrine-specific proteins and which they designated NSP. The original cDNA was identified by screening an expression library of the small-cell lung cancer (SCLC) NCI-H82 cell line with antibodies to the previously identified proteins. The gene can produce 3 different transcripts (3.4, 2.3, and 1.8 kb), which are identical at their 3-prime ends but have unique amino termini. The common carboxyl-terminal region contains 2 large hydrophobic domains. The largest cDNA (NSP-A) produces a 135-kD (776-amino acid) protein which is rich in proline and serine residues and contains multiple potential phosphoryla-

tion sites. NSP-B and NSP-C have predicted reading frames of 356 and 208 amino acids, respectively. The B transcript is found only in the NCI-H82 cell line. NSP-specific antibodies showed that the proteins are localized to membranes of the endoplasmic reticulum (Senden et al., 1994), leading to their proposed designation as 'reticulons.' Immunohistochemical studies in the rat (van de Velde et al., 1994) showed the presence of NSP-A protein in many regions of the brain. NSP-A or -C transcripts were found in 18 different SCLC lines but not in any of 11 nonendocrine non-SCLCs (van de Velde et al., 1994). Kools et al. (1994) mapped the human NSP gene to 14q21-q22 by fluorescence in situ hybridization Roebroek et al. (1996) found that the NSP exons are dispersed over a genomic region of about 275 kb. The genomic organization explained the generation of NSP mRNA variants encoding NSP protein isoforms. Multiple promoters rather than alternative splicing of internal exons seemed to be involved in this diversity. Comparison of NSP genomic and cDNA sequences with databank nucleotide sequences resulted in the discovery of other human members of this novel family of reticulon encoding genes

[17612] Full details of the abovementioned studies are described

in the following publications, the disclosure of which are hereby incorporated by reference:

- [17613] van de Velde, H. J. K.; Roebroek, A. J. M.; van Leeuwen, F. W.; Van de Ven, W. J. M. : Molecular analysis of expression in rat brain of NSP-A, a novel neuroendocrine-specific protein of the endoplasmic reticulum. *Molec. Brain Res.* 23: 81-92, 1994. ; and
- [17614] Roebroek, A. J. M.; Ayoubi, T. A. Y.; van de Velde, H. J. K.; Schoenmakers, E. F. P. M.; Pauli, I. G. L.; Van de Ven, W. J. M. : Genomic organization of the human NSP gene, prototype of a.
- [17615] Further studies establishing the function and utilities of RTN1 are found in John Hopkins OMIM database record ID 600865, and in cited publications numbered 7016-7021 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Secreted Frizzled-related Protein 1 (SFRP1, Accession NM_003012) is another VGAM337 host target gene. SFRP1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SFRP1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SFRP1 BIND-

ING SITE, designated SEQ ID:8934, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17616] Another function of VGAM337 is therefore inhibition of Secreted Frizzled-related Protein 1 (SFRP1, Accession NM_003012), a gene which is a receptor for wnt proteins that may have an anti-apoptotic function. Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SFRP1. The function of SFRP1 and its association with various diseases and clinical conditions, has been established by previous studies, as described hereinabove with reference to VGAM250. Calneuron 1 (CALN1, Accession NM_031468) is another VGAM337 host target gene. CALN1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by CALN1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of CALN1 BINDING SITE, designated SEQ ID:25514, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17617] Another function of VGAM337 is therefore inhibition of Calneuron 1 (CALN1, Accession NM_031468). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with CALN1. DNAM-1 (Accession NM_006566) is another VGAM337 host target gene. DNAM-1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by DNAM-1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DNAM-1 BINDING SITE, designated SEQ ID:13341, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17618] Another function of VGAM337 is therefore inhibition of DNAM-1 (Accession NM_006566). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DNAM-1. EZFIT (Accession NM_021216) is another VGAM337 host target gene. EZFIT BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by EZFIT, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III.

Table 2 illustrates the complementarity of the nucleotide sequences of EZFIT BINDING SITE, designated SEQ ID:22198, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17619] Another function of VGAM337 is therefore inhibition of EZFIT (Accession NM_021216). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with EZFIT. KIAA1500 (Accession XM_034353) is another VGAM337 host target gene. KIAA1500 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1500, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1500 BINDING SITE, designated SEQ ID:32065, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17620] Another function of VGAM337 is therefore inhibition of KIAA1500 (Accession XM_034353). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with

KIAA1500. SEF (Accession XM_045300) is another VGAM337 host target gene. SEF BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by SEF, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEF BINDING SITE, designated SEQ ID:34426, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17621] Another function of VGAM337 is therefore inhibition of SEF (Accession XM_045300). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEF. Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869) is another VGAM337 host target gene. SEZ6 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by SEZ6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of SEZ6 BINDING SITE, designated SEQ ID:36773, to the nucleotide sequence of VGAM337 RNA, herein designated

VGAM RNA, also designated SEQ ID:3048.

[17622] Another function of VGAM337 is therefore inhibition of Seizure Related 6 Homolog (mouse) (SEZ6, Accession XM_058869). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with SEZ6. LOC221477 (Accession XM_166397) is another VGAM337 host target gene. LOC221477 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221477, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221477 BINDING SITE, designated SEQ ID:44260, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17623] Another function of VGAM337 is therefore inhibition of LOC221477 (Accession XM_166397). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC221477. LOC50999 (Accession NM_016040) is another VGAM337 host target gene. LOC50999 BINDING SITE is HOST TARGET binding site found in the 3' un-

translated region of mRNA encoded by LOC50999, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC50999 BINDING SITE, designated SEQ ID:18116, to the nucleotide sequence of VGAM337 RNA, herein designated VGAM RNA, also designated SEQ ID:3048.

[17624] Another function of VGAM337 is therefore inhibition of LOC50999 (Accession NM_016040). Accordingly, utilities of VGAM337 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC50999. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 338 (VGAM338) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17625] VGAM338 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM338 was detected is described hereinabove with reference to Figs. 1–8.

[17626] VGAM338 gene, herein designated VGAM GENE, is a viral

gene contained in the genome of Saimiriine Herpesvirus 2. VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17627] VGAM338 gene encodes a VGAM338 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM338 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM338 precursor RNA is designated SEQ ID:324, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:324 is located at position 21425 relative to the genome of Saimiriine Herpesvirus 2.

[17628] VGAM338 precursor RNA folds onto itself, forming VGAM338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17629] An enzyme complex designated DICER COMPLEX, `dices` the VGAM338 folded precursor RNA into VGAM338 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM338 RNA is designated SEQ ID:3049, and is provided hereinbelow with reference to the sequence listing part.

[17630] VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM338 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17631] VGAM338 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. This

complementary binding is due to the fact that the nucleotide sequence of VGAM338 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM338 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17632] The complementary binding of VGAM338 RNA, herein designated VGAM RNA, to host target binding sites on VGAM338 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM338 host tar-

get RNA into VGAM338 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17633] It is appreciated that VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM338 host target genes. The mRNA of each one of this plurality of VGAM338 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM338 RNA, herein designated VGAM RNA, and which when bound by VGAM338 RNA causes inhibition of translation of respective one or more VGAM338 host target proteins.

[17634] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM338 gene, herein designated VGAM GENE, on one or more VGAM338 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4

and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17635] It is yet further appreciated that a function of VGAM338 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM338 correlate with, and may be deduced from, the identity of the host target genes which VGAM338 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17636] Nucleotide sequences of the VGAM338 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM338 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM338 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM338 are further

described hereinbelow with reference to Table 1.

[17637] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM338 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM338 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17638] As mentioned hereinabove with reference to Fig. 1, a function of VGAM338 gene, herein designated VGAM is inhibition of expression of VGAM338 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM338 correlate with, and may be deduced from, the identity of the target genes which VGAM338 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17639] Nuclear Transcription Factor Y, Gamma (NFYC, Accession NM_014223) is a VGAM338 host target gene. NFYC BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by NFYC, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of NFYC

BINDING SITE, designated SEQ ID:15492, to the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, also designated SEQ ID:3049.

[17640] A function of VGAM338 is therefore inhibition of Nuclear Transcription Factor Y, Gamma (NFYC, Accession NM_014223). Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with NFYC. KIAA0042 (Accession NM_014875) is another VGAM338 host target gene. KIAA0042 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0042, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0042 BINDING SITE, designated SEQ ID:17014, to the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, also designated SEQ ID:3049.

[17641] Another function of VGAM338 is therefore inhibition of KIAA0042 (Accession NM_014875). Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0042. KIAA0322 (Accession XM_166591) is another

VGAM338 host target gene. KIAA0322 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA0322, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA0322 BINDING SITE, designated SEQ ID:44559, to the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, also designated SEQ ID:3049.

[17642] Another function of VGAM338 is therefore inhibition of KIAA0322 (Accession XM_166591). Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA0322. LOC115400 (Accession XM_055880) is another VGAM338 host target gene. LOC115400 BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by LOC115400, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC115400 BINDING SITE, designated SEQ ID:36348, to the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, also designated SEQ ID:3049.

[17643] Another function of VGAM338 is therefore inhibition of LOC115400 (Accession XM_055880). Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC115400. LOC51701 (Accession NM_016231) is another VGAM338 host target gene. LOC51701 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51701, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51701 BINDING SITE, designated SEQ ID:18346, to the nucleotide sequence of VGAM338 RNA, herein designated VGAM RNA, also designated SEQ ID:3049.

[17644] Another function of VGAM338 is therefore inhibition of LOC51701 (Accession NM_016231). Accordingly, utilities of VGAM338 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51701. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 339 (VGAM339) viral gene, which modulates expression of respective host target genes thereof,

the function and utility of which host target genes is known in the art.

[17645] VGAM339 is a novel bioinformatically detected regulatory, non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM339 was detected is described hereinabove with reference to Figs. 1–8.

[17646] VGAM339 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Saimiriine Herpesvirus 2. VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17647] VGAM339 gene encodes a VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM339 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM339 precursor RNA is designated SEQ ID:325, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:325 is located at position 22382 relative to the genome of Saimiriine Herpesvirus 2.

[17648] VGAM339 precursor RNA folds onto itself, forming VGAM339 folded precursor RNA, herein designated VGAM

FOLDED PRECURSOR RNA, which has a two-dimensional
`hairpin structure`. As is well known in the art, this
`hairpin structure`, is typical of RNA encoded by miRNA
genes, and is due to the fact that the nucleotide sequence
of the first half of the RNA encoded by a miRNA gene is an
accurate or partial inversed-reversed sequence of the nu-
cleotide sequence of the second half thereof.

[17649] An enzyme complex designated DICER COMPLEX, `dices`
the VGAM339 folded precursor RNA into VGAM339 RNA,
herein designated VGAM RNA, a single stranded ~22 nt
long RNA segment. As is known in the art, `dicing` of a
hairpin structured RNA precursor product into a short
~22nt RNA segment is catalyzed by an enzyme complex
comprising an enzyme called Dicer together with other
necessary proteins. A probable (over 41%) nucleotide se-
quence of VGAM339 RNA is designated SEQ ID:3050, and
is provided hereinbelow with reference to the sequence
listing part.

[17650] VGAM339 host target gene, herein designated VGAM
HOST TARGET GENE, encodes a corresponding messenger
RNA, VGAM339 host target RNA, herein designated VGAM
HOST TARGET RNA. VGAM339 host target RNA comprises
three regions, as is typical of mRNA of a protein coding

gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17651] VGAM339 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM339 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM339 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in

the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17652] The complementary binding of VGAM339 RNA, herein designated VGAM RNA, to host target binding sites on VGAM339 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM339 host target RNA into VGAM339 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17653] It is appreciated that VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM339 host target genes. The mRNA of each one of this plurality of VGAM339 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM339 RNA, herein designated VGAM RNA, and which when bound by VGAM339 RNA causes inhibition of translation of respective one or more VGAM339 host target proteins.

[17654] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by

VGAM339 gene, herein designated VGAM GENE, on one or more VGAM339 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17655] It is yet further appreciated that a function of VGAM339 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of viral infection by Saimiriine Herpesvirus 2. Specific functions, and accordingly utilities, of VGAM339 correlate with, and may be deduced from, the identity of the host target genes which VGAM339 binds and inhibits, and the function of these host target genes, as elaborated

hereinbelow.

- [17656] Nucleotide sequences of the VGAM339 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the `diced` VGAM339 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM339 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM339 are further described hereinbelow with reference to Table 1.
- [17657] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM339 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM339 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.
- [17658] As mentioned hereinabove with reference to Fig. 1, a function of VGAM339 gene, herein designated VGAM is inhibition of expression of VGAM339 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM339 correlate with, and may be deduced from, the identity of the target genes which VGAM339 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17659] Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218) is a VGAM339 host target gene. KCNQ1 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KCNQ1, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KCNQ1 BINDING SITE, designated SEQ ID:5723, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17660] A function of VGAM339 is therefore inhibition of Potassium Voltage-gated Channel, KQT-like Subfamily, Member 1 (KCNQ1, Accession NM_000218), a gene which probably important in cardiac repolarization. associates with kcne1 (mink) to form the i(ks) cardiac potassium current. elicits a rapidly activating, k(+)-selective outward current. muscarinic agonist oxotremorine-m strongly suppresses kcnq1/kcne1 current in cho cells in which cloned kcnq1/kcne1 channels were coexpressed with m1 muscarinic receptors. may associate also with kcne3 (mirp2) to form the potassium channel that is important for cyclic amp-stimulated intestinal secretion of chloride

io TISSUE:abondantly expressed in heart, pancreas, prostate, kidney, small intestine and peripheral blood leukocytes. less abondant in placenta, lung, spleen, colon, thymus, testis and ovaries. Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KCNQ1. The function of KCNQ1 has been established by previous studies. Congenital long QT syndrome (LQTS) is electrocardiographically characterized by a prolonged QT interval and polymorphic ventricular arrhythmias (torsade de pointes). These cardiac arrhythmias may result in recurrent syncope, seizure, or sudden death. Mutation in the KCNQ1 gene can cause either Romano-Ward syndrome or Jervell and Lange-Nielsen syndrome (OMIM Ref. No. 220400). The candidate gene approach had been used to identify genes responsible for long QT syndrome on chromosome 7 (OMIM Ref. No. 152427) and chromosome 3 (OMIM Ref. No. 600163). Wang et al. (1996) used positional cloning methods to establish a gene, which they called KVLQT1, as the chromosome 11-linked LQT1 gene. KVLQT1 is strongly expressed in the heart and codes a protein with structural features of a voltage-gated potassium channel. The longest open reading frame of the

KVLQT1 cDNA spans 1,645 bp. The authors found KVLQT1 mutations in affected members of 16 arrhythmia families, including 1 intragenic deletion and 10 different missense mutations (e.g., 192500.0001). Marx et al. (2002) demonstrated that beta-adrenergic receptor modulation of the slow outward potassium ion current (I-KS) requires targeting of cAMP-dependent protein kinase A (OMIM Ref. No. 188830) and protein phosphatase 1 (PP1; e.g., 176875) to KCNQ1 through the targeting protein yotiao (OMIM Ref. No. 604001). Yotiao binds to KCNQ1 by a leucine zipper motif, which is disrupted by an LQTS mutation (KCNQ1-G589D; 192500.0029). Identification of the KCNQ1 macromolecular complex provides a mechanism for sympathetic nervous system modulation of cardiac action potential duration through I-KS. Animal model experiments lend further support to the function of KCNQ1. To produce a mouse model for Jervell and Lange-Nielsen syndrome, Casimiro et al. (2001) generated a line of transgenic mice that had a targeted disruption in the Kcnq1 gene. Behavioral analysis demonstrated that the homozygous null mice were deaf and exhibited a shaker-waltzer phenotype. Histologic analysis of the inner ear structures of these mice showed gross morphologic

anomalies because of drastic reduction in the volume of endolymph. ECGs recorded from the null mice demonstrated abnormal T- and P-wave morphologies and prolongation of the QT and JT intervals when measured in vivo, but not in isolated hearts. These changes were indicative of cardiac repolarization defects that appear to be induced by extracardiac signals.

[17661] It is appreciated that the abovementioned animal model for KCNQ1 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17662] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17663] Marx, S. O.; Kurokawa, J.; Reiken, S.; Motoike, H.; D'Armiento, J.; Marks, A. R.; Kass, R. S. : Requirement of a macromolecular signaling complex for beta adrenergic receptor modulation of the KCNQ1-KCNE1 potassium channel. Science 295: 496-499, 2002. ; and

[17664] Casimiro, M. C.; Knollmann, B. C.; Ebert, S. N.; Vary, J. C., Jr.; Greene, A. E.; Franz, M. R.; Grinberg, A.; Huang, S. P.; Pfeifer, K. : Targeted disruption of the Kcnq1 gene produces.

[17665] Further studies establishing the function and utilities of KCNQ1 are found in John Hopkins OMIM database record ID 192500, and in cited publications numbered 5747-5749, 10835-5774, 1498, 2199-2200, 1497, 1499-1513, 10836-1522, 5777, 6058-6061, 2209, 2210, 6062-6067, 10837-6075, 2216, 6076-781, 4332-78 and 2222 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961) is another VGAM339 host target gene. PTGIS BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by PTGIS, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of PTGIS BINDING SITE, designated SEQ ID:6667, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17666] Another function of VGAM339 is therefore inhibition of Prostaglandin I₂ (prostacyclin) Synthase (PTGIS, Accession NM_000961), a gene which catalyzes the isomerization of prostaglandin h₂ to prostacyclin (= prostaglandin i₂). Accordingly, utilities of VGAM339 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with PTGIS. The function of PTGIS and its association with various diseases and clinical conditions, has been established by previous studies, as described herein above with reference to VGAM206. HSPC065 (Accession NM_014157) is another VGAM339 host target gene. HSPC065 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by HSPC065, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of HSPC065 BINDING SITE, designated SEQ ID:15450, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17667] Another function of VGAM339 is therefore inhibition of HSPC065 (Accession NM_014157). Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of diseases and clinical conditions associated with HSPC065. LOC148760 (Accession XM_097514) is another VGAM339 host target gene. LOC148760 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC148760, corresponding to a HOST

TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC148760 BINDING SITE, designated SEQ ID:40898, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17668] Another function of VGAM339 is therefore inhibition of LOC148760 (Accession XM_097514). Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC148760. LOC221773 (Accession XM_165802) is another VGAM339 host target gene. LOC221773 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC221773, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC221773 BINDING SITE, designated SEQ ID:43761, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17669] Another function of VGAM339 is therefore inhibition of LOC221773 (Accession XM_165802). Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment

of diseases and clinical conditions associated with LOC221773. LOC51696 (Accession NM_016217) is another VGAM339 host target gene. LOC51696 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOC51696, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOC51696 BINDING SITE, designated SEQ ID:18310, to the nucleotide sequence of VGAM339 RNA, herein designated VGAM RNA, also designated SEQ ID:3050.

[17670] Another function of VGAM339 is therefore inhibition of LOC51696 (Accession NM_016217). Accordingly, utilities of VGAM339 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOC51696. Fig. 1 further provides a conceptual description of a novel bioinformatically detected viral gene of the present invention, referred to here as Viral Genomic Address Messenger 340 (VGAM340) viral gene, which modulates expression of respective host target genes thereof, the function and utility of which host target genes is known in the art.

[17671] VGAM340 is a novel bioinformatically detected regulatory,

non protein coding, viral micro RNA (miRNA) gene. The method by which VGAM340 was detected is described hereinabove with reference to Figs. 1–8.

[17672] VGAM340 gene, herein designated VGAM GENE, is a viral gene contained in the genome of Tobacco Mosaic Virus. VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, is a human gene contained in the human genome.

[17673] VGAM340 gene encodes a VGAM340 precursor RNA, herein designated VGAM PRECURSOR RNA. Similar to other miRNA genes, and unlike most ordinary genes, VGAM340 precursor RNA does not encode a protein. A nucleotide sequence identical or highly similar to the nucleotide sequence of VGAM340 precursor RNA is designated SEQ ID:326, and is provided hereinbelow with reference to the sequence listing part. Nucleotide sequence SEQ ID:326 is located at position 3101 relative to the genome of Tobacco Mosaic Virus.

[17674] VGAM340 precursor RNA folds onto itself, forming VGAM340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, which has a two-dimensional `hairpin structure`. As is well known in the art, this `hairpin structure`, is typical of RNA encoded by miRNA

genes, and is due to the fact that the nucleotide sequence of the first half of the RNA encoded by a miRNA gene is an accurate or partial inversed-reversed sequence of the nucleotide sequence of the second half thereof.

[17675] An enzyme complex designated DICER COMPLEX, `dices` the VGAM340 folded precursor RNA into VGAM340 RNA, herein designated VGAM RNA, a single stranded ~22 nt long RNA segment. As is known in the art, `dicing` of a hairpin structured RNA precursor product into a short ~22nt RNA segment is catalyzed by an enzyme complex comprising an enzyme called Dicer together with other necessary proteins. A probable (over 40%) nucleotide sequence of VGAM340 RNA is designated SEQ ID:3051, and is provided hereinbelow with reference to the sequence listing part.

[17676] VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, encodes a corresponding messenger RNA, VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. VGAM340 host target RNA comprises three regions, as is typical of mRNA of a protein coding gene: a 5` untranslated region, a protein coding region and a 3` untranslated region, designated 5`UTR, PROTEIN CODING and 3`UTR respectively.

[17677] VGAM340 RNA, herein designated VGAM RNA, binds complementarily to one or more host target binding sites located in untranslated regions of VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. This complementary binding is due to the fact that the nucleotide sequence of VGAM340 RNA is an accurate or a partial inversed-reversed sequence of the nucleotide sequence of each of the host target binding sites. As an illustration, Fig. 1 shows three such host target binding sites, designated BINDING SITE I, BINDING SITE II and BINDING SITE III respectively. It is appreciated that the number of host target binding sites shown in Fig. 1 is meant as an illustration only, and is not meant to be limiting – VGAM340 RNA, herein designated VGAM RNA, may have a different number of host target binding sites in untranslated regions of a VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA. It is further appreciated that while Fig. 1 depicts host target binding sites in the 3`UTR region, this is meant as an example only – these host target binding sites may be located in the 3`UTR region, the 5`UTR region, or in both 3`UTR and 5`UTR regions.

[17678] The complementary binding of VGAM340 RNA, herein

designated VGAM RNA, to host target binding sites on VGAM340 host target RNA, herein designated VGAM HOST TARGET RNA, such as BINDING SITE I, BINDING SITE II and BINDING SITE III, inhibits translation of VGAM340 host target RNA into VGAM340 host target protein, herein designated VGAM HOST TARGET PROTEIN. VGAM host target protein is therefore outlined by a broken line.

[17679] It is appreciated that VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, in fact represents a plurality of VGAM340 host target genes. The mRNA of each one of this plurality of VGAM340 host target genes comprises one or more host target binding sites, each having a nucleotide sequence which is at least partly complementary to VGAM340 RNA, herein designated VGAM RNA, and which when bound by VGAM340 RNA causes inhibition of translation of respective one or more VGAM340 host target proteins.

[17680] It is further appreciated by one skilled in the art that the mode of translational inhibition illustrated by Fig. 1 with specific reference to translational inhibition exerted by VGAM340 gene, herein designated VGAM GENE, on one or more VGAM340 host target gene, herein designated VGAM HOST TARGET GENE, is in fact common to other

known non-viral miRNA genes. As mentioned hereinabove with reference to the background section, although a specific complementary binding site has been demonstrated only for some of the known miRNA genes (primarily Lin-4 and Let-7), all other recently discovered miRNA genes are also believed by those skilled in the art to modulate expression of other genes by complementary binding, although specific complementary binding sites of these other miRNA genes have not yet been found (Ruvkun G., `Perspective: Glimpses of a tiny RNA world`, Science 294,779 (2001)).

[17681] It is yet further appreciated that a function of VGAM340 is inhibition of expression of host target genes, as part of a novel viral mechanism of attacking a host. Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of viral infection by Tobacco Mosaic Virus. Specific functions, and accordingly utilities, of VGAM340 correlate with, and may be deduced from, the identity of the host target genes which VGAM340 binds and inhibits, and the function of these host target genes, as elaborated hereinbelow.

[17682] Nucleotide sequences of the VGAM340 precursor RNA, herein designated VGAM PRECURSOR RNA, and of the

`diced` VGAM340 RNA, herein designated VGAM RNA, and a schematic representation of the secondary folding of VGAM340 folded precursor RNA, herein designated VGAM FOLDED PRECURSOR RNA, of VGAM340 are further described hereinbelow with reference to Table 1.

[17683] Nucleotide sequences of host target binding sites, such as BINDING SITE-I, BINDING SITE-II and BINDING SITE-III of Fig. 1, found on VGAM340 host target RNA, and schematic representation of the complementarity of each of these host target binding sites to VGAM340 RNA, herein designated VGAM RNA, are described hereinbelow with reference to Table 2.

[17684] As mentioned hereinabove with reference to Fig. 1, a function of VGAM340 gene, herein designated VGAM is inhibition of expression of VGAM340 target genes. It is appreciated that specific functions, and accordingly utilities, of VGAM340 correlate with, and may be deduced from, the identity of the target genes which VGAM340 binds and inhibits, and the function of these target genes, as elaborated hereinbelow.

[17685] Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286) is a VGAM340 host target gene. AQP6 BINDING SITE is HOST TARGET binding site found in the 5` un-

translated region of mRNA encoded by AQP6, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of AQP6 BINDING SITE, designated SEQ ID:27610, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17686] A function of VGAM340 is therefore inhibition of Aquaporin 6, Kidney Specific (AQP6, Accession NM_053286), a gene which participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism. Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with AQP6. The function of AQP6 has been established by previous studies. Ma et al. (1997), who referred to this gene as aquaporin-6 (AQP6), demonstrated that, among the 7 human aquaporins cloned to that time (AQPs 0 to 6), the genes encoding the 4 most closely related aquaporins all mapped to 12q13: AQP0, AQP2, AQP5 (OMIM Ref. No. 600442), and AQP6. To construct a physical map and identify novel aquaporin gene members of this cluster, Ma et al. (1997) screened a human CEPH B YAC library by PCR using

primers derived from exon 4 of the AQP2 and AQP0 genes. A YAC clone with 200 kb of human DNA was isolated and analyzed. Primary pulsed field gel electrophoresis and Southern blot analysis indicated the presence of AQP2, AQP5, and AQP6 genes, but not AQP0. Restriction mapping and PCR analysis yielded a precise physical map in which the 3 aquaporin genes spanned only approximately 27 kb with the order, transcription orientation, and spacer length as follows: 5-prime--AQP2--5kb spacer--AQP5--7kb spacer--AQP6--3-prime. Yasui et al. (1999) showed that AQP6 is localized exclusively in intracellular membranes in renal epithelia. Sequential ultracentrifugation of rat kidney homogenates confirmed that AQP6 resides predominantly in vesicular fractions, and immunohistochemical and immunoelectron microscopic studies confirmed that more than 98% of AQP6 is located in intracellular membrane vesicles. In glomeruli, AQP6 is present in membrane vesicles within podocyte cell bodies and foot processes. In proximal tubules, AQP6 is also abundant in membrane vesicles within the subapical compartment of segment 2 and segment 3 cells, but was not detected in the brush border or basolateral membranes. In collecting duct, AQP6 resides in intracellular membrane vesicles in

apical, mid, and basolateral cytoplasm of type A intercalated cells, but was not observed in the plasma membrane. Unlike other members of the AQP family, the unique distribution in intracellular membrane vesicles in multiple types of renal epithelia indicated that AQP6 is not simply involved in transcellular fluid absorption. These studies predicted that AQP6 participates in distinct physiologic function such as glomerular filtration, tubular endocytosis, and acid-base metabolism.

[17687] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17688] Ma, T.; Yang, B.; Umenishi, F.; Verkman, A. S. : Closely spaced tandem arrangement of AQP2, AQP5, and AQP6 genes in a 27-kilobase segment at chromosome locus 12q13. *Genomics* 43: 387–389, 1997. ; and

[17689] Yasui, M.; Kwon, T.-H.; Knepper, M. A.; Nielsen, S.; Agre, P. : Aquaporin-6: an intracellular vesicle water channel protein in renal epithelia. *Proc. Nat. Acad. Sci.* 96: 5808–5813, 1999.

[17690] Further studies establishing the function and utilities of AQP6 are found in John Hopkins OMIM database record ID 601383, and in cited publications numbered 717 and

7178 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326) is another VGAM340 host target gene. MAPRE3 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by MAPRE3, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of MAPRE3 BINDING SITE, designated SEQ ID:14717, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17691] Another function of VGAM340 is therefore inhibition of Microtubule-associated Protein, RP/EB Family, Member 3 (MAPRE3, Accession NM_012326), a gene which interact with cytoplasmic microtubules, and with the adenomatous polyposis coli. Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with MAPRE3. The function of MAPRE3 has been established by previous studies. EB1 family proteins (e.g., MAPRE1; 603108) interact with cytoplasmic microtubules in interphase cells, with mitotic

spindles, and with the adenomatous polyposis coli (APC; 175100) tumor suppressor gene. Using a yeast 2-hybrid screen with the C terminus of APC-like (APCL) as bait, Nakagawa et al. (2000) isolated a cDNA encoding MAPRE3, which they termed EB3. The predicted 282-amino acid protein is 54% identical to MAPRE1. Northern blot analysis revealed expression of a 2.2-kb transcript predominantly in brain and muscle. GST pull-down analysis determined that a homologous region in the C termini of APC and APCL binds to MAPRE3. Immunofluorescence and confocal microscopy demonstrated that MAPRE3 is localized in the microtubule network and colocalizes with APCL in the perinucleus and microtubule network. By EST database searching, RT-PCR, and screening a fetal brain cDNA library, Su and Qi (2001) isolated a cDNA encoding a protein identical to the EB3 protein reported by Nakagawa et al. (2000), which they termed EBF3, and an alternative transcript encoding a 266-amino acid protein. RT-PCR and Western blot analyses indicated that both transcripts are ubiquitously expressed. Genomic sequence analysis showed that there are most likely 3 MAPRE genes: MAPRE1 encodes EB1; MAPRE2 (OMIM Ref. No. 605789) encodes RP1 and the EB2 fragment; and MAPRE3 encodes EBF3 and

the fragment RP3. MAPRE3, like MAPRE1 and MAPRE2, contains 7 exons, but the coding region of MAPRE3 spans only 4.2 kb due to relatively short introns. Western blot analysis detected expression of both isoforms as approximately 32-kD proteins in most cell lines tested. Binding analysis determined that both isoforms interact with APC. By FISH, Nakagawa et al. (2000) mapped the MAPRE3 gene to 2p23.3–p23.1. Using radiation hybrid analysis, Su and Qi (2001) mapped the MAPRE3 gene to 2p23.3–p23.2, where it is closely linked and proximal to the ketohexokinase gene (OMIM Ref. No. 229800).

[17692] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17693] Nakagawa, H.; Koyama, K.; Murata, Y.; Morito, M.; Akiyama, T.; Nakamura, Y. : EB3, a novel member of the EB1 family preferentially expressed in the central nervous system, binds to a CNS-specific APC homologue. *Onco-gene* 19: 210–216, 2000. ; and

[17694] Su, L.-K.; Qi, Y. : Characterization of human MAPRE genes and their proteins. *Genomics* 71: 143–149, 2001.

[17695] Further studies establishing the function and utilities of MAPRE3 are found in John Hopkins OMIM database record

ID 605788, and in cited publications numbered 628 and 8578 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. RAB23, Member RAS Oncogene Family (RAB23, Accession NM_016277) is another VGAM340 host target gene. RAB23 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by RAB23, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of RAB23 BINDING SITE, designated SEQ ID:18401, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17696] Another function of VGAM340 is therefore inhibition of RAB23, Member RAS Oncogene Family (RAB23, Accession NM_016277), a gene which is involved in the regulation of intracellular membrane trafficking. Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with RAB23. The function of RAB23 has been established by previous studies. Rab proteins are small GTPases of the Ras superfamily involved in the regulation of intracellular membrane trafficking. For additional background information

on Rab proteins, see 179508. The RAB23 gene encodes an essential negative regulator of the Sonic hedgehog (SHH; 600725) signaling pathway. Animal model experiments lend further support to the function of RAB23. Mouse embryos homozygous for mutations in the 'open brain' (opb) gene die during the second half of gestation, with an open neural tube in the head and spinal cord, abnormal somites, polydactyly, and poorly developed eyes. The opb1 allele encodes a lys-to-ter mutation at codon 39; the opb2 allele encodes an arg-to-ter mutation at codon 80. These alleles would lack the domains required for guanine nucleotide and Rab effector binding and are therefore null alleles.

[17697] It is appreciated that the abovementioned animal model for RAB23 is acknowledged by those skilled in the art as a scientifically valid animal model, as can be further appreciated from the publications cited hereinbelow.

[17698] Full details of the abovementioned studies are described in the following publications, the disclosure of which are hereby incorporated by reference:

[17699] Eggenschwiler, J. T.; Espinoza, E.; Anderson, K. V. : Rab23 is an essential negative regulator of the mouse Sonic hedgehog signalling pathway. Nature 412: 194–198,

2001. ; and

[17700] Zhang, Q.-H.; Ye, M.; Wu, X.-Y.; Ren, S.-X.; Zhao, M.; Zhao, C.-J.; Fu, G.; Shen, Y.; Fan, H.-Y.; Lu, G.; Zhong, M.; Xu, X.-R.; and 9 others : Cloning and functional analysis of cDNAs w.

[17701] Further studies establishing the function and utilities of RAB23 are found in John Hopkins OMIM database record ID 606144, and in cited publications numbered 6472-6473 listed in the bibliography section hereinbelow, which are also hereby incorporated by reference. Apolipoprotein L, 4 (APOL4, Accession NM_030643) is another VGAM340 host target gene. APOL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by APOL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of APOL4 BINDING SITE, designated SEQ ID:24976, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17702] Another function of VGAM340 is therefore inhibition of Apolipoprotein L, 4 (APOL4, Accession NM_030643). Accordingly, utilities of VGAM340 include diagnosis, preven-

tion and treatment of diseases and clinical conditions associated with APOL4. DKFZP564G092 (Accession NM_015601) is another VGAM340 host target gene. DKFZP564G092 BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by DKFZP564G092, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of DKFZP564G092 BINDING SITE, designated SEQ ID:17876, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17703] Another function of VGAM340 is therefore inhibition of DKFZP564G092 (Accession NM_015601). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with DKFZP564G092. FLJ00001 (Accession XM_088525) is another VGAM340 host target gene. FLJ00001 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of mRNA encoded by FLJ00001, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of

FLJ00001 BINDING SITE, designated SEQ ID:39771, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17704] Another function of VGAM340 is therefore inhibition of FLJ00001 (Accession XM_088525). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ00001. FLJ10846 (Accession NM_018241) is another VGAM340 host target gene. FLJ10846 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by FLJ10846, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ10846 BINDING SITE, designated SEQ ID:20200, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17705] Another function of VGAM340 is therefore inhibition of FLJ10846 (Accession NM_018241). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ10846. FLJ11539 (Accession NM_024748) is another VGAM340 host target gene. FLJ11539 BINDING SITE is HOST TARGET

binding site found in the 3' untranslated region of mRNA encoded by FLJ11539, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of FLJ11539 BINDING SITE, designated SEQ ID:24088, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17706] Another function of VGAM340 is therefore inhibition of FLJ11539 (Accession NM_024748). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with FLJ11539. Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640) is another VGAM340 host target gene. GGA2 BINDING SITE1 and GGA2 BINDING SITE2 are HOST TARGET binding sites found in untranslated regions of mRNA encoded by GGA2, corresponding to HOST TARGET binding sites such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of GGA2 BINDING SITE1 and GGA2 BINDING SITE2, designated SEQ ID:28922 and SEQ ID:17401 respectively, to the nucleotide sequence of VGAM340 RNA,

herein designated VGAM RNA, also designated SEQ ID:3051.

[17707] Another function of VGAM340 is therefore inhibition of Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2, Accession NM_138640). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with GGA2. KIAA1546 (Accession XM_042301) is another VGAM340 host target gene. KIAA1546 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by KIAA1546, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of KIAA1546 BINDING SITE, designated SEQ ID:33712, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17708] Another function of VGAM340 is therefore inhibition of KIAA1546 (Accession XM_042301). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with KIAA1546. Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211) is another VGAM340 host target gene.

LOXL4 BINDING SITE is HOST TARGET binding site found in the 3' untranslated region of mRNA encoded by LOXL4, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of LOXL4 BINDING SITE, designated SEQ ID:25928, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17709] Another function of VGAM340 is therefore inhibition of Lysyl Oxidase-like 4 (LOXL4, Accession NM_032211). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with LOXL4. Serine/threonine Kinase 17b (apoptosis-inducing) (STK17B, Accession NM_004226) is another VGAM340 host target gene. STK17B BINDING SITE is HOST TARGET binding site found in the 5' untranslated region of mRNA encoded by STK17B, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of STK17B BINDING SITE, designated SEQ ID:10421, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM

RNA, also designated SEQ ID:3051.

[17710] Another function of VGAM340 is therefore inhibition of Serine/threonine Kinase 17b (apoptosis-inducing) (STK17B, Accession NM_004226). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with STK17B. TUSP (Accession NM_020245) is another VGAM340 host target gene. TUSP BINDING SITE is HOST TARGET binding site found in the 5` untranslated region of mRNA encoded by TUSP, corresponding to a HOST TARGET binding site such as BINDING SITE I, BINDING SITE II or BINDING SITE III. Table 2 illustrates the complementarity of the nucleotide sequences of TUSP BINDING SITE, designated SEQ ID:21518, to the nucleotide sequence of VGAM340 RNA, herein designated VGAM RNA, also designated SEQ ID:3051.

[17711] Another function of VGAM340 is therefore inhibition of TUSP (Accession NM_020245). Accordingly, utilities of VGAM340 include diagnosis, prevention and treatment of diseases and clinical conditions associated with TUSP. LOC169611 (Accession XM_095809) is another VGAM340 host target gene. LOC169611 BINDING SITE is HOST TARGET binding site found in the 3` untranslated region of